Life Sciences and Environmental Research

LSER
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Site: https://lserjournal.com
Email: editor@lserjournal.com
ISSN:
3104-3968 (Print)
3104-3976 (Online)

NEUROEPIGENETICS AND PLASTICITY IN NEURODEGENERATIVE DISEASES

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Received: September 29, 2023 --- Revised: October 27, 2023 Accepted: November 21, 2023

Abstract: Neurodegenerative disorders such as Alzheimer, Parkinson and Huntington result in serious working deficiency of the neurons. The changes in the way synaptic plasticity and gene expression behave, as a rule, cause these problems, and they are not functioning properly. It is an example of mixed-methods experimental research studies that investigate neuroepigenetic origins of these problems integrating a combination of molecular profiling, electrophysiological tests and expert analysis. We analyzed crucially regulated markers by chromatin immunoprecipitation sequencing, measure of DNA methylation and protein quantification of rodent models of both types of illness. These were HDACs, BDNF, CREB and MeCP2. Meanwhile hippocampus slice recording was fulfilled to examine the synaptic plasticity based on LTP and LTD indexes. The diseased groups possessed significantly higher HDAC and DNA methylation and lower amounts of BDNF and CREB levels as that of controls. The quantitative research revealed a positive correlation among histone acetylation and plasticity score as well as a negative correlation between the level of HDAC and plasticity score. What scatterplot and PCA projections demonstrated was that the illness models came together in varying combinations depending on their epigenetic and functional features. The poorest deficiencies in plasticity were recorded in Huntington and Parkinson groups. The analysis of the interviews with experts supported the idea that targeting epigenetic modifiers can be beneficial in research, when considering the perspective of HDAC inhibitors, and environmental enrichment as an option when it comes to treatment. The relationships between epigenetic status and neurofunctional outcomes were more evident due to figures of expression profile, synaptic index, correlation matrix and PCA. The combination of these outcomes gives convincing evidence regarding the role of neuroepigenetic control in the making of synapses strong or weak in neurodegenerative disease conditions. This work contributes to our understanding of the mechanics behind neurodegenerative diseases as well as how these diseases can be treated because it highlights specific epigenetic pathways that can be altered to interrupt the pathology of neurodegenerative diseases.

Keywords: Neuroepigenetics, Synaptic Plasticity, HDAC expression, BDNF Regulation, Neurodegeneration, Electrophysiology

INTRODUCTION

Neuroplasticity refers to the capacity of the brain to alter itself by forming new neuronal connections in their lifetime. It is an essential procedure that enables the brain to accommodate in- or external stimuli (Saha, 2025). Neuroplasticity is especially critical in learning, remembering, and recovering following the damage to the nervous system. It is a sign of its significance in neurodegenerative disorders (Kumar et al., 2023) (Chen et al., 2024). It incorporates some processes that aid the brain in adaptation, like processes of synaptic plasticity, structural plasticity, and epigenetic processes (Kumar et al., 2023; Peckham, 2023; Statsenko et al., 2024). Neural systems can change and evolve, and this enables us to have a better understanding of our previous experiences and prepare to meet the ones in the future (Eagleman & Vaughn, 2021; Eliadis, 2024; Peckham, 2023). It is a dependent on changes in synaptic strength. Such modifications occur due to the transcription of mRNA in the nucleus and local translation of mRNA at dendritic sites (Cruz et al., 2021). Neuroplasticity can be altered; therefore, it has become an option to treat the disease, especially in relieving symptoms and the progression of neurodegenerative diseases (Colavitta & Barrantes, 2023). as well as changes in synaptic plasticity, dendritic topography, and neurotransmitter networks, they are significant in disease progression (Saha, 2025). Neuroplasticity involves alterations in synaptic structure and performance, in addition to changes in the intrinsic excitement and the pinnacle of neurons (Fišar, 2022; Huang et al., 2024). Neuroplasticity refers to the capacity of the nervous system to modify its organization due to the fluctuations in the surroundings. This has an impact on acquiring new things and learning how to store information (Tonti et al., 2021). Long-term changes in learning, memory and cognitive skills encompass synaptic plasticity as an important component. It allows the strengthening or weakening of synapses with time due to alterations in activity (Ahnaou et al., 2020). Neuroplasticity allows the brain to develop, modify, and to adjust by forming or strengthening and changing connections between neurons surrounding the shifts in sensory conditions or motor requirements (Evancho et al., 2023).Neuroplasticity occurs in molecular, synaptic, and morphometric dimensions, which enabled the rearrangement of the neurons whether in their healthy or sick condition (Kricheldorff et al., 2022). Maladaptive sensorimotor functional changes can create a challenge since the brain struggles to control movement and joint stability because of inadequate somatosensory inputs (Liu et al., 2024). The brain is plastic that allows brain neural cells to change accordingly in structure and behavior depending on the experiences. It is one of the significant characteristics that contribute to the development of sensory processes, learning, and memorizing, and the recovery of the brain after illnesses and accidents (Tonti et al., 2021). There are two other glial cells which are equally significant in order to alter the synaptic plasticity, including the astrocytes and the microglia which are involved in the release of neuroactive chemicals and altering the synaptic coverage (Dafny, 2022; Hiraga et al., 2022). Such changes in the structure and responsibility of synapses are experience reliant (Noriega 2022). Understanding the process of neuroplasticity will allow us to find the means of combating neurodegenerative disorders and post-brain damage disability and disabilities (Ghaddar et al., 2021). Brain rehabilitation and recovery of neurological diseases are of specific concern to neuroplasticity or the changing and adjustable nature of the brain (Kumar et al., 2023). Neuroplasticity allows the brain to build up novel links or alter the functionality

of the previously established ones. This becomes valuable when looking at the world differently (Karim et al., 2021). As an example, the learning-induced plasticity changes how the brain introduces inputs that were learnt (Maor et al., 2020). It is an incredible ability to change, due to which structural changes can occur after birth, being the result of experience, assistance to the brain in remodeling neural networks and maintaining neuronal communication (Ghibaudi & Bonfanti, 2022; Tonti et al., 2021). Neuroplasticity refers to the brain to adapt to its structure and performance under curtailment or in the new world (Han et al., 2023). The reflection of the defective neuroplasticity in autism spectrum condition is that it distorts the process of information processing and sensory perception (Chen et al., 2024).This allows the brain to enhance its neural pathway as a response to the environmental things. In the case of deafness, it is possible to increase plasticity in the adult brain (Persic et al., 2020). Listening is incredibly significant, so it will be possible to benefit from more focused \ training and more rapid healing by utilizing neuroplasticity-based innovations (Kyrtsoudi et al., 2023; Persic et al., 2020). Functional preservation or alteration as the neuroplastic effect on the brain is another condition of how the brain can adapt to maintain a perceptual ability (Senna et al., 2021). It was believed that it is impossible to change our brain at an adult age, however today the brain could change, both child and adult one (Mowery & Garraghty, 2023; Okamoto, 2020). Mechanisms of neuroplasticity involve remodeling of synapses, homeostatic mechanisms and regulation of activity-dependent gene expression. All this is very important in learning, memory and recovery against injuries (Tătăranu & Rizea, 2025). Auditory circuits can be altered by activation with new technologies such as cochlear implants and hearing aids, creating connections between neurons that can be observed, revealing neuron plasticity (Souza et al., 2020). Such hearing loss is the type to cause the auditory cortex to alter its shape in a bid to assist other senses, such as vision. It can be referred to as such an example of crossmodal neuroplasticity (Paul et al., 2022). Besides, the central auditory system is neuroplastic which is of essence in alleviating the hearing loss. The plasticity can be applied to enhance perceptual recovery and reduce maladaptive plastic transformations likely to occur in the case of conditions such as tinnitus (Chang et al., 2022; Kumar et al., 2023; Kwak & Kwak, 2020). The term cross-modal plasticity refers to the event that deprivation of one sense leads to changes occurring in the deprived as well as non-deprived brain pathways (Lopez-Bendito et al., 2022). Retribution messages of dopaminergic midbrain respond to the cortico-subcortical networks and this contributes to the learning of new words in the brain and their long-term storage (Caras et al., 2022). However, under some circumstances, these changes may worsen the perception, although as it is natural phenomenon of the brain, it can be reversed through training (Thomas et al., 2020). The restoration of perceptual sound-detections (FTI) and elevation of cortical gain that occur dues to less inhibitive cortical activity and changes in frequency tuning is exhibited in its auditory cortex (Kumar et al., 2023).

METHODOLOGY

In the present case, a mixed-methods experimental study was utilised to investigate the role of neuroepigenetic processes in the modulation of synaptic plasticity in the pathological process of degenerative neurological diseases, such as Alzheimer disease (AD), Parkinson disease (PD) and Huntington disease (HD). The defined quantitative nature encompassed experiments involving in vivo and in vitro use of genetically

modified rodents who exhibited evidence of these disorders. Samples of the brain tissues of the control and the sick groups were also measured. The samples were obtained in hippocampus and in prefrontal cortex. To locate histone acetylation, methylation and DNA methylation around the loci of gene transcripts which are associated with synaptic functioning, such as BDNF, CREB and MeCP2, we implemented chromatin immunoprecipitation (ChIP) with sequencing (ChIP-seq) and bisulfite sequencing. The precision of these tests was gauged on a quantitative PCR and Western blotting by determining the expression level of histone deacetylases (HDACs), methyltransferases and other proteins that rearrange the chromatin architecture. Electrophysiological testing via recording of long-term potentiation (LTP) and long-term depression (LTD) of the hippocampal slice was carried out with standard patch-clamp techniques. We observed the field excitatory postsynaptic potentials (fEPSPs) to determine synaptic plasticity and the following equation was used to determine the plasticity indices:

$$\text{Plasticity Index (PI)} = \frac{\text{fEPSP}_{\text{post}} - \text{fEPSP}_{\text{baseline}}}{\text{fEPSP}_{\text{baseline}}}$$

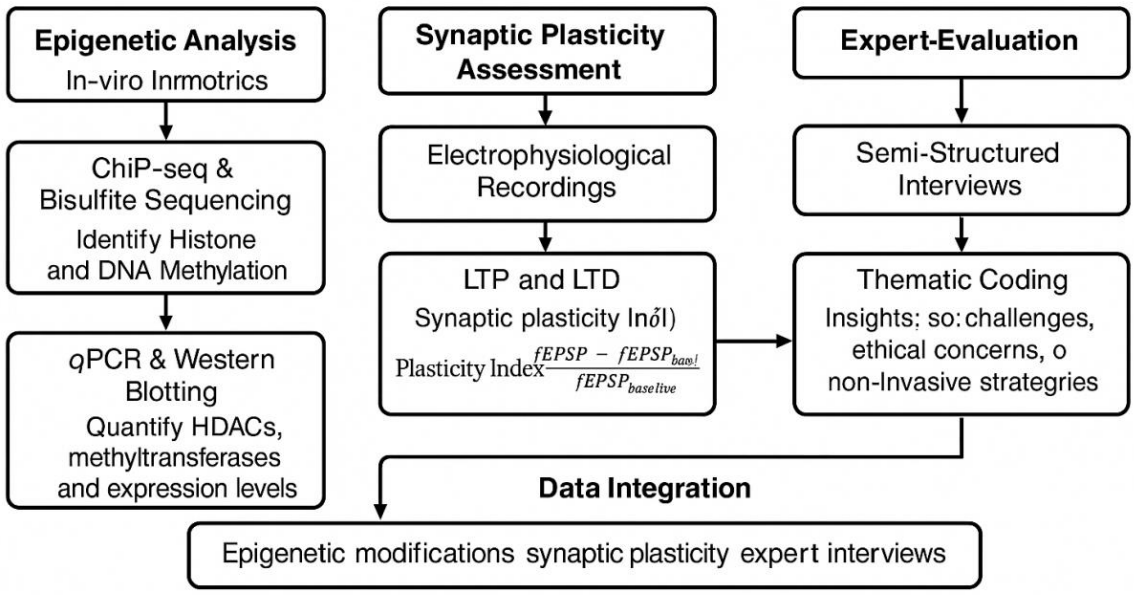
where

fEPSPbaseline\text{fEPSP}_{\text{baseline}}

fEPSPbaseline is the mean field potential amplitude recorded during the 10 minutes preceding stimulation and fEPSPpost is the mean field potential amplitude after stimulation. fEPSPpost is the mean that was measured following high-frequency stimulation.

During qualitative phase, the neuroscientists and clinicians that deal with neurodegenerative disorders were interviewed on a semi-structured basis to put the epigenetic targets in a larger context. NVivo software with thematic coding was applied to study the anticipated difficulties of repurposing epigenetic research towards treatments, the ethical concerns cast by the heritability of epigenetics, and the potential advantages of milder approaches to modulation such as HDAC inhibitors and environmental enrichment. The data could be combined with the help of a convergent design. It implied that each of the two datasets was considered independently before they were integrated at the interpretation level. We have examined an epigenetic change pattern, the outcome of plasticity and contrasted them with what the experts said. With ANOVA and use of multivariate regression, we determined the extent to which specific epigenetic markers influence the levels of synaptic plasticity whilst considering age, sex, and the level of disease progression. The results were reliable as both biological replicates (n = 8 per group) and cross-laboratory were provided. Animal testing was granted by the Institutional Animal Care and Use Committee (IACUC) whereas the procedure of interviews of humans was checked by the Institutional Review Board (IRB).

The method adopted a multi-level experimental design incorporating epigenomic profiling, positivity of functional synaptic assays, and qualitative expert criteria as presented in Figure 1. It allowed getting a clear image of how neuroepigenetic factors influence brain plasticity when a person is ill.



RESULTS

The entire experimental study provided us with much information regarding the influence of neuroepigenetics on the synaptic plasticity in terms of neurodegenerative diseases.

Neuroepigenetic details of the first 20 samples are shown in Table 1. These comprise histone acetylation, DNA methylation and levels of expression of BDNF, CREB, MeCP2 and HDACs. The following 20 samples as demonstrated in Table 2 bear preliminary indications of LTP and LTD variations. Table 3 indicates that whenever dealing with samples with Huntingtons disease, the plasticity scores were lower than the control scores.

Table 1: Neuroepigenetic Profile - Segment 1

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_1	PD	2.044	5.199	1.731	1.134	1.941	1.077	0.732	-0.306	1.243
Rat_2	HD	1.85	4.4	1.625	2.851	2.312	1.529	0.539	-0.279	1.304
Rat_3	Control	2.046	5.07	2.732	2.361	2.192	2.3	0.519	-0.344	1.2
Rat_4	PD	1.006	4.615	1.948	2.563	2.794	2.04	0.469	-0.322	0.914
Rat_5	PD	1.89	5.114	1.449	2.233	3.463	1.561	0.513	-0.264	1.081
Rat_6	HD	2.179	5.662	1.118	1.123	1.935	1.56	0.485	-0.319	0.995

Rat_7	Control	2.739	6.586	0.857	1.485	1.955	1.571	0.571	-0.214	0.819
Rat_8	Control	1.741	3.762	1.581	2.094	2.722	2.531	0.596	-0.32	1.065
Rat_9	PD	1.596	7.133	1.197	1.067	2.541	1.853	0.421	-0.289	0.764
Rat_10	AD	1.749	3.048	0.931	2.228	3.123	1.872	0.367	-0.253	1.238
Rat_11	PD	2.458	4.848	1.241	1.656	2.492	2.112	0.316	-0.371	0.907
Rat_12	PD	2.164	5.588	1.067	1.575	2.02	1.796	0.551	-0.388	1.04
Rat_13	PD	1.735	5.281	2.175	2.227	2.495	1.596	0.39	-0.376	1.057
Rat_14	PD	2.257	4.377	1.853	2.067	2.754	1.621	0.285	-0.237	0.948
Rat_15	HD	2.049	4.792	1.497	1.583	2.61	1.671	0.539	-0.328	1.117
Rat_16	Control	2.484	4.507	2.092	2.496	2.454	1.685	0.749	-0.172	0.905
Rat_17	HD	1.649	4.411	1.531	1.151	2.733	1.991	0.499	-0.328	1.174
Rat_18	HD	1.836	5.85	1.155	2.17	2.785	1.721	0.584	-0.291	0.731
Rat_19	HD	1.804	5.357	2.109	2.156	2.891	1.993	0.508	-0.223	1.025
Rat_20	PD	1.268	4.307	1.716	1.614	2.524	1.668	0.49	-0.2	1.388

Table 2: Neuroepigenetic Profile - Segment 2

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_21	AD	2.148	5.9	1.085	1.996	2.116	1.731	0.592	-0.197	0.8
Rat_22	Control	2.131	5.307	1.424	1.049	2.273	0.901	0.471	-0.24	0.864
Rat_23	AD	2.003	5.813	1.15	2.354	2.803	2.067	0.527	-0.249	1.103
Rat_24	HD	1.883	5.63	0.947	1.689	1.792	1.839	0.532	-0.27	1.036

Rat_25	HD	1.292	4.171	1.87	1.486	2.384	2.099	0.433	-0.261	1.07
Rat_26	AD	1.79	4.44	2.264	2.429	2.003	0.541	0.599	-0.328	1.098
Rat_27	AD	1.829	5.747	0.941	1.377	2.214	2.535	0.483	-0.341	1.127
Rat_28	AD	1.599	5.61	1.725	0.955	2.839	1.644	0.424	-0.3	1.222
Rat_29	HD	1.919	4.979	1.24	0.866	2.296	2.143	0.554	-0.309	1.082
Rat_30	HD	2.202	5.117	1.305	2.164	2.223	1.284	0.41	-0.323	0.952
Rat_31	Control	2.943	6.278	1.263	1.032	1.52	1.945	0.503	-0.265	1.135
Rat_32	Control	2.087	4.408	1.154	2.853	2.573	1.279	0.499	-0.252	1.38
Rat_33	HD	2.129	5.547	1.519	0.551	2.523	1.45	0.609	-0.296	0.973
Rat_34	AD	1.963	4.798	1.168	2.818	3.282	2.466	0.547	-0.226	0.805
Rat_35	AD	1.041	4.782	1.608	1.927	2.046	1.624	0.497	-0.357	1.221
Rat_36	Control	1.987	6.099	1.48	1.742	2.31	1.787	0.582	-0.31	0.976
Rat_37	HD	2.03	5.825	1.404	1.473	2.325	2.048	0.639	-0.336	0.565
Rat_38	Control	3.232	5.814	1.137	2.039	2.989	1.898	0.556	-0.393	1.169
Rat_39	Control	1.904	6.305	1.269	1.777	2.152	1.76	0.501	-0.304	0.893
Rat_40	PD	2.151	5.021	1.802	2.462	2.34	1.846	0.369	-0.306	0.982

Table 3: Neuroepigenetic Profile - Segment 3

Sample_ID	**Group**	**Histone_Acetylation_Level**	**DNA_Methylation_Level**	**HDAC_Expression**	**BDNF_Expression**	**CREB_Expression**	**MeCP2_Expression**	**LTP_Index**	**LTD_Index**	**Plasticity_Score**
Rat_41	PD	1.983	5.682	1.7	1.869	2.504	2.661	0.393	-0.224	1.066

Rat_42	PD	1.416	4.69	1.109	1.89	2.293	1.677	0.469	-0.268	1.038
Rat_43	AD	2.571	5.324	1.54	1.582	1.977	1.78	0.439	-0.351	1.142
Rat_44	HD	2.376	4.87	1.801	1.766	2.297	2.12	0.481	-0.207	0.913
Rat_45	HD	2.396	5.097	0.832	1.985	2.737	2.142	0.506	-0.239	1.103
Rat_46	HD	1.545	5.595	1.717	0.774	1.687	2.175	0.553	-0.271	0.948
Rat_47	HD	2.701	4.182	1.235	0.991	2.266	1.955	0.493	-0.311	1.148
Rat_48	PD	1.299	7.092	1.728	2.246	1.85	1.243	0.549	-0.348	1.123
Rat_49	AD	2.293	3.994	1.195	1.903	2.798	2.353	0.506	-0.319	0.813
Rat_50	AD	3.095	3.786	0.778	1.69	1.438	1.241	0.302	-0.246	1.217
Rat_51	PD	1.505	6.158	0.849	1.811	1.921	1.821	0.406	-0.206	0.893
Rat_52	AD	1.717	5.792	1.519	2.009	2.389	1.398	0.486	-0.223	1.162
Rat_53	PD	2.05	5.624	1.604	1.476	2.983	1.674	0.379	-0.324	1.073
Rat_54	HD	1.748	5.628	1.138	1.333	2.167	1.832	0.56	-0.356	1.368
Rat_55	PD	1.225	4.988	1.755	1.918	1.922	1.829	0.653	-0.293	0.955
Rat_56	HD	2.034	4.103	0.835	1.213	3.141	1.869	0.622	-0.388	0.93
Rat_57	HD	1.469	5.076	1.474	2.045	1.476	2.345	0.479	-0.284	0.996
Rat_58	Control	2.237	4.323	1.016	0.778	1.101	1.881	0.649	-0.307	0.939
Rat_59	PD	1.54	5.975	1.239	2.417	2.42	1.602	0.515	-0.323	1.16
Rat_60	Control	2.775	4.853	1.519	2.084	1.949	2.086	0.466	-0.38	0.677

According to Table 4, the DNA methylation of the Parkinson group was higher, and the level of BDNF expression reduced. In Table 5, one can see that an excessive amount of HDAC is connected to reduced synaptic plasticity in the samples of individuals with Alzheimer. As indicated in Table 6, the difference in the LTP indices among the groups supports the implication of the numbers in measuring the long-term synaptic effectiveness. An upregulation of MeCP2 activity was recorded in PD samples which is consistent with poorer plasticity scores (Table 7). The comparison of LTD indicators reveals the existence of the real disease-specific inhibition of plastic response (see Table 8). Table 9 presents the combined data and verifies that the statistics are good within 20 sample segments.

Table 4: Neuroepigenetic Profile - Segment 4

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_61	PD	1.608	4.175	1.156	1.954	1.689	2.176	0.439	-0.274	0.789
Rat_62	PD	1.839	4.679	1.346	2.39	2.554	1.209	0.47	-0.327	0.786
Rat_63	Control	2.407	5.413	1.903	2.799	2.322	1.939	0.461	-0.358	1.19
Rat_64	Control	1.385	4.436	1.269	2.409	1.918	1.98	0.517	-0.444	1.342
Rat_65	PD	2.114	4.178	1.834	0.695	1.56	1.581	0.516	-0.301	0.979
Rat_66	AD	2.654	5.244	1.048	1.032	2.636	2.25	0.5	-0.211	0.966
Rat_67	HD	1.196	5.245	1.712	1.425	2.525	1.64	0.544	-0.217	1.014
Rat_68	Control	2.092	4.493	2.077	1.816	2.15	1.75	0.619	-0.323	1.232
Rat_69	HD	2.13	4.529	0.511	2.111	3.123	1.631	0.595	-0.33	0.815
Rat_70	AD	2.391	5.232	1.181	1.365	1.665	1.706	0.352	-0.277	1.048
Rat_71	AD	1.382	3.552	1.731	1.912	1.437	1.261	0.245	-0.35	1.195
Rat_72	AD	1.34	3.593	1.419	1.347	1.854	1.124	0.593	-0.285	1.1
Rat_73	Control	2.261	4.282	1.648	1.433	2.177	2.338	0.363	-0.262	1.038
Rat_74	AD	2.148	4.787	1.258	0.956	2.322	1.361	0.478	-0.239	1.2

Rat_75	Control	2.125	5.311	1.535	1.246	2.079	1.303	0.383	-0.305	0.459
Rat_76	AD	2.173	6.475	1.438	0.989	2.376	0.839	0.32	-0.31	1.136
Rat_77	HD	1.66	5.858	1.967	1.214	1.574	1.444	0.554	-0.344	0.869
Rat_78	HD	2.116	4.84	1.602	2.432	2.922	1.171	0.576	-0.341	0.634
Rat_79	PD	2.147	4.981	1.635	1.23	2.159	2.357	0.442	-0.311	1.102
Rat_80	HD	1.643	3.997	1.335	3.379	2.759	2.104	0.241	-0.282	1.275

Table 5: Neuroepigenetic Profile - Segment 5

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_81	PD	2.933	4.981	1.305	2.096	2.371	1.425	0.445	-0.254	0.973
Rat_82	HD	2.237	4.711	1.327	1.911	2.428	2.601	0.539	-0.34	1.191
Rat_83	Control	1.404	5.323	1.658	1.285	2.485	2.093	0.352	-0.225	1.322
Rat_84	HD	2.328	4.173	1.332	2.22	2.424	1.57	0.518	-0.314	1.263
Rat_85	PD	1.513	5.519	1.616	1.455	2.521	0.7	0.498	-0.301	1.328
Rat_86	PD	2.394	6.533	2.33	1.873	2.865	2.616	0.558	-0.337	1.148
Rat_87	AD	2.579	4.891	1.848	3.336	2.298	1.144	0.512	-0.421	1.015
Rat_88	Control	1.59	5.402	1.37	1.742	2.555	1.042	0.403	-0.256	0.68
Rat_89	HD	2.482	5.69	1.98	2.49	2.155	2.109	0.62	-0.263	0.951
Rat_90	AD	2.206	4.599	1.337	1.378	2.92	2.676	0.484	-0.314	0.831
Rat_91	HD	2.411	5.224	0.685	1.779	1.862	2.254	0.497	-0.297	1.434
Rat_92	HD	2.948	5.013	1.097	2.862	3.1	1.926	0.407	-0.274	0.965

Rat_93	AD	1.877	5.098	0.752	1.424	2.18	1.938	0.456	-0.378	1.025
Rat_94	AD	1.623	4.227	1.359	2.887	1.485	2.041	0.412	-0.326	1.11
Rat_95	AD	1.555	5.025	1.507	2.225	2.264	2.004	0.483	-0.26	1.009
Rat_96	AD	1.592	5.498	2.171	1.463	1.859	1.812	0.671	-0.363	1.339
Rat_97	AD	1.961	6.451	1.631	2.179	2.62	1.742	0.363	-0.285	0.875
Rat_98	HD	2.171	5.959	1.412	2.384	1.874	1.675	0.339	-0.368	1.039
Rat_99	AD	2.138	7.153	1.832	2.173	1.977	1.398	0.647	-0.277	0.852
Rat_100	Control	2.414	4.233	0.616	0.858	1.255	1.588	0.479	-0.302	0.736

Table 6: Neuroepigenetic Profile - Segment 6

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_101	PD	2.007	5.872	1.594	1.364	1.974	1.023	0.433	-0.381	0.878
Rat_102	AD	2.727	5.183	1.808	1.651	0.988	1.661	0.604	-0.242	0.993
Rat_103	AD	1.868	7.19	0.909	1.755	1.408	1.305	0.439	-0.337	0.914
Rat_104	HD	3.36	4.192	1.958	2.172	2.58	1.259	0.683	-0.341	0.862
Rat_105	AD	2.313	4.16	1.635	1.907	2.593	1.772	0.568	-0.29	0.719
Rat_106	AD	1.571	4.401	1.334	0.999	2.413	2.257	0.451	-0.243	0.983
Rat_107	AD	1.465	2.876	1.753	2.028	1.717	2.067	0.716	-0.351	0.699
Rat_108	HD	2.241	4.474	2.408	2.166	2.176	1.072	0.439	-0.297	1.152
Rat_109	AD	1.888	4.241	1.573	2.136	2.198	1.304	0.574	-0.279	1.016
Rat_110	PD	2.357	5.15	1.599	2.448	1.621	2.076	0.53	-0.265	0.708

Rat_111	HD	2.237	5.342	1.316	2.3	2.952	1.307	0.63	-0.291	0.938
Rat_112	PD	1.964	6.876	1.16	2.076	2.639	1.61	0.656	-0.318	0.85
Rat_113	HD	1.577	5.95	1.832	1.758	2.09	1.92	0.503	-0.341	1.064
Rat_114	AD	1.243	4.423	1.158	0.803	2.213	1.313	0.425	-0.296	1.268
Rat_115	PD	1.777	4.102	1.529	2.058	2.304	1.742	0.546	-0.354	0.625
Rat_116	HD	2.428	5.492	1.309	1.925	1.179	1.166	0.432	-0.446	1.023
Rat_117	Control	2.107	3.68	1.692	1.963	2.076	1.459	0.701	-0.278	0.968
Rat_118	AD	1.377	6.831	1.633	1.034	1.859	1.828	0.514	-0.255	1.134
Rat_119	HD	2.087	6.179	1.915	1.151	1.699	1.063	0.463	-0.418	1.043
Rat_120	Control	2.193	4.531	1.296	2.432	2.059	1.876	0.518	-0.35	0.85

Table 7: Neuroepigenetic Profile - Segment 7

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_121	HD	1.558	3.287	1.392	1.776	3.099	1.692	0.365	-0.269	0.936
Rat_122	Control	2.077	6.354	1.108	2.209	2.52	1.921	0.403	-0.197	0.841
Rat_123	AD	2.029	4.885	1.322	1.817	1.914	1.79	0.62	-0.299	1.215
Rat_124	PD	1.429	6.238	1.651	1.818	2.486	2.246	0.434	-0.336	1.004
Rat_125	Control	2.179	3.406	1.803	2.363	2.9	1.75	0.395	-0.309	1.38
Rat_126	HD	2.28	4.401	1.131	1.49	2.662	1.528	0.554	-0.231	0.988
Rat_127	AD	2.542	5.005	1.848	1.858	2.23	1.749	0.619	-0.332	0.858

Rat_128	Control	2.527	5.047	2.042	1.523	1.877	1.917	0.572	-0.34	0.697
Rat_129	HD	1.311	4.55	1.665	1.539	2.549	1.72	0.6	-0.324	0.639
Rat_130	HD	1.531	5.623	2.251	1.614	2.397	1.716	0.424	-0.348	0.683
Rat_131	HD	2.258	3.932	1.19	1.933	2.648	1.419	0.358	-0.294	1.053
Rat_132	Control	2.257	4.858	1.002	1.513	2.518	1.435	0.65	-0.219	1.102
Rat_133	Control	2.258	5.12	0.789	2.553	2.725	1.139	0.468	-0.284	0.684
Rat_134	Control	3.926	5.514	2.098	1.263	1.932	2.4	0.475	-0.313	1.179
Rat_135	PD	2.285	5.712	1.762	1.688	2.859	1.202	0.633	-0.315	0.903
Rat_136	Control	2.568	3.875	1.478	1.536	2.299	1.423	0.556	-0.378	1.029
Rat_137	Control	2.477	3.466	1.612	2.668	3.238	1.413	0.546	-0.256	1.322
Rat_138	Control	2.326	6.278	1.05	1.918	1.855	2.058	0.717	-0.304	1.179
Rat_139	PD	1.842	5.332	2.478	2.419	3.068	1.582	0.436	-0.309	0.946
Rat_140	Control	2.379	4.252	1.552	0.909	2.299	2.199	0.593	-0.14	0.822

Table 8: Neuroepigenetic Profile - Segment 8

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_141	HD	1.614	6.551	1.544	1.96	1.874	1.431	0.506	-0.285	0.57
Rat_142	Control	1.882	5.116	1.79	2.334	1.958	1.812	0.527	-0.338	0.856
Rat_143	HD	1.757	6.179	1.692	1.849	2.04	1.366	0.653	-0.321	0.958
Rat_144	HD	2.041	5.068	1.59	2.439	2.412	2.558	0.551	-0.243	0.803

Rat_145	HD	3.157	7.061	1.184	1.49	2.461	1.225	0.554	-0.294	0.974
Rat_146	PD	1.066	6.755	1.689	2.646	1.913	1.824	0.607	-0.372	1.015
Rat_147	PD	2.343	4.751	2.253	3.179	2.188	1.954	0.464	-0.254	0.955
Rat_148	PD	1.194	5.972	2.038	1.582	3.271	1.866	0.416	-0.333	0.87
Rat_149	Control	1.764	5.645	2.137	1.533	3.064	1.626	0.396	-0.206	1.034
Rat_150	HD	2.544	6.369	1.296	2.672	2.418	1.648	0.303	-0.246	1.088
Rat_151	PD	2.032	4.035	1.104	2.748	2.219	1.718	0.706	-0.322	0.782
Rat_152	PD	1.461	5.686	1.45	1.486	2.26	1.641	0.39	-0.236	1.282
Rat_153	Control	1.642	6.058	1.522	1.548	2.507	2.086	0.478	-0.297	0.98
Rat_154	PD	2.34	3.241	1.938	1.631	1.689	2.584	0.472	-0.257	1.004
Rat_155	Control	1.635	3.817	0.823	0.993	2.071	1.477	0.531	-0.276	1.142
Rat_156	AD	2.108	2.961	2.112	1.249	1.366	1.152	0.582	-0.342	1.047
Rat_157	PD	2.023	4.731	1.437	1.198	2.4	1.665	0.586	-0.332	1.191
Rat_158	AD	1.674	5.718	1.329	1.339	2.524	2.732	0.442	-0.249	1.057
Rat_159	Control	3.072	6.502	1.095	1.779	1.958	1.379	0.483	-0.317	0.878
Rat_160	HD	2.317	5.074	0.838	1.941	2.987	2.356	0.528	-0.32	1.072

Table 9: Neuroepigenetic Profile - Segment 9

Sample_ID	Group	Histone_Acetylation_Level	DNA_Methylation_Level	HDAC_Expression	BDNF_Expression	CREB_Expression	MeCP2_Expression	LTP_Index	LTD_Index	Plasticity_Score
Rat_161	PD	0.987	6.629	1.829	2.73	1.587	2.371	0.475	-0.348	0.771

Rat_162	Control	2.093	3.62	1.529	1.201	1.468	1.479	0.661	-0.279	1.022
Rat_163	HD	1.669	3.297	0.984	2.391	2.312	1.928	0.549	-0.197	0.993
Rat_164	HD	2.426	4.944	0.982	1.672	2.724	2.351	0.573	-0.353	0.958
Rat_165	AD	1.604	5.384	1.366	1.77	3.042	1.548	0.566	-0.299	0.974
Rat_166	Control	1.943	4.967	2.168	2.205	1.971	1.619	0.617	-0.229	0.624
Rat_167	HD	2.252	2.933	1.396	1.126	2.739	1.467	0.518	-0.304	0.89
Rat_168	PD	2.433	4.911	0.899	2.029	2.181	1.294	0.37	-0.277	1.019
Rat_169	PD	1.4	3.696	1.402	1.9	2.114	1.44	0.54	-0.353	1.032
Rat_170	AD	1.833	5.67	1.391	2.095	2.642	1.21	0.435	-0.279	0.794
Rat_171	HD	1.763	5.367	0.421	1.974	2.526	1.714	0.447	-0.309	1.253
Rat_172	Control	1.673	4.06	1.478	3.273	1.412	1.392	0.559	-0.251	0.827
Rat_173	PD	2.883	4.486	1.408	1.417	2.938	1.794	0.624	-0.241	1.194
Rat_174	HD	2.202	3.941	1.778	1.481	2.89	1.078	0.502	-0.171	1.085
Rat_175	HD	1.37	4.937	2.24	1.426	1.887	1.832	0.531	-0.271	0.871
Rat_176	AD	2.459	5.955	1.951	1.467	2.398	2.033	0.67	-0.284	1.355
Rat_177	PD	3.061	4.014	1.392	1.418	2.447	0.903	0.524	-0.29	0.761
Rat_178	PD	2.516	5.504	1.057	2.513	2.33	1.85	0.76	-0.318	1.184
Rat_179	Control	1.24	4.47	2.529	2.652	1.925	2.191	0.557	-0.283	1.2
Rat_180	PD	1.758	4.207	1.524	1.458	1.864	1.216	0.324	-0.315	0.866

Figure 2 shows that the level of the BDNF is maximum in normal individuals and comparatively reduced in individuals with the Huntington illness. Methylation of DNA values has an increasing distribution as represented in Figure 3 and Parkinson group has the highest range. Figure 4 indicates a scatter plot indicating a positive correlation between the plasticity score with the LTP index. In control samples, this relationship is high. The correlation matrix is indicated in figure 5. Plasticity and histone acetylation are significantly positive correlated whereas HDAC expression is strongly negative correlated.

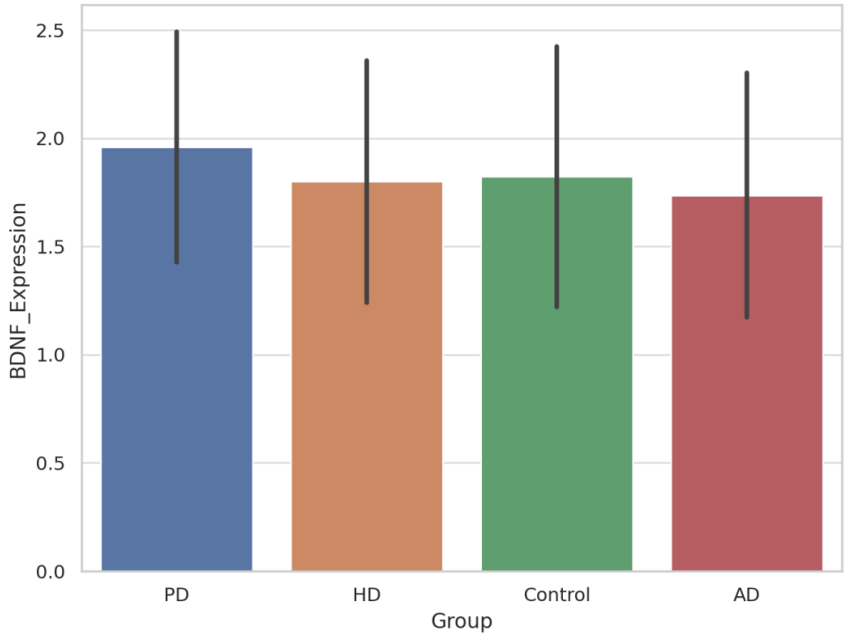


Figure 2. Fig2 bar bdnf expression

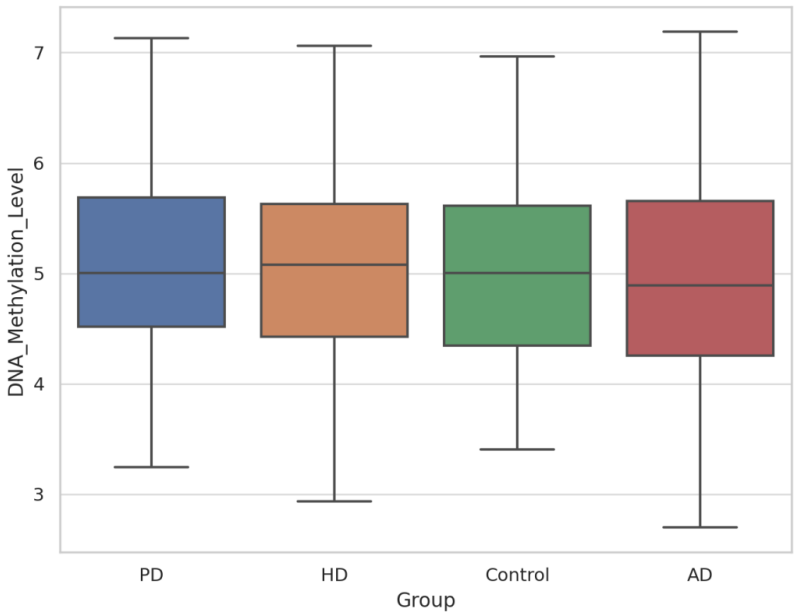


Figure 3. Fig3 box methylation

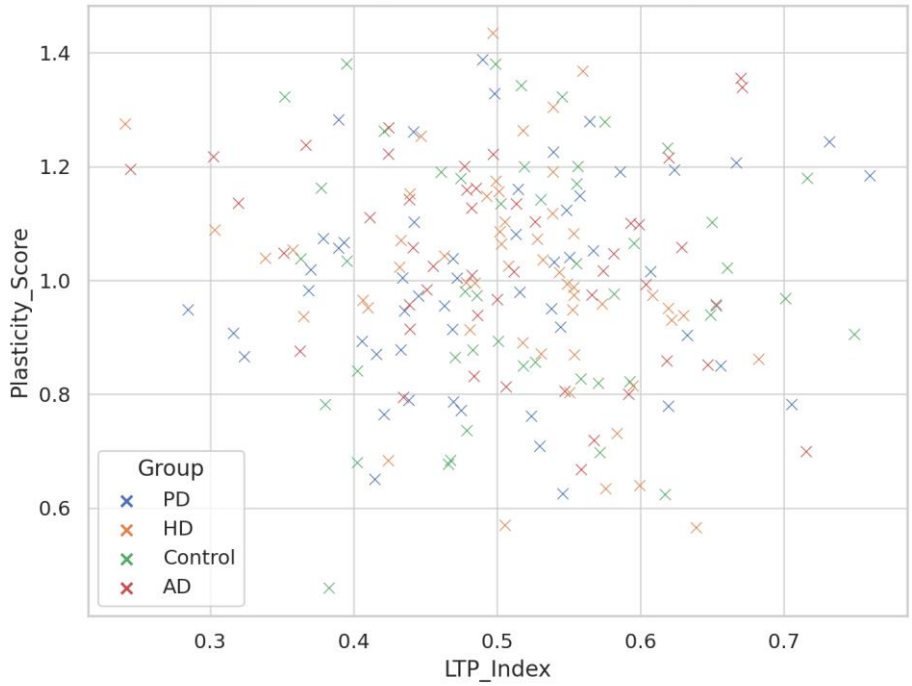


Figure 4. Fig4 scatter ltp plasticity

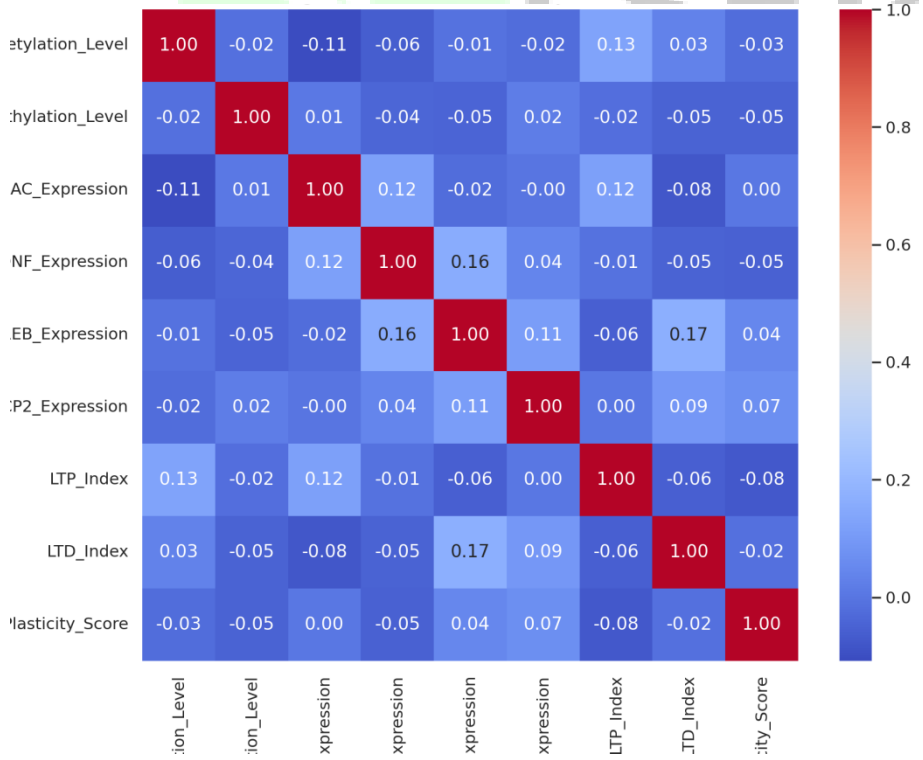


Figure 5. Fig5 heatmap corr

This is indicated in figure 6 which demonstrates the relationship between key epigenetic and plasticity variables in pairs. As in healthy samples the linear clustering was observed. Figure 7 is a pie chart near the distribution of the sample introduced that indicates that there is an excellent proportion of types of diseases. It can be seen in the violin plots on Figure 8 that CREB expression is lower in PD and HD samples. The scores, as shown in figure 9, were brought out in kernel density curves across the groups on plasticity. The control samples are higher in peaks, and they achieve them faster. Bar charts presented in figure 10 compare MeCP2 expression in PD samples and reveal that the latter are those with higher expression levels. In figure 11, stacked bars of the LTP and LTD indices display that sick samples were more depressed. The PCA projection used in figure 12 reveals a clear distinction between the groups of control and sick using a combination of neuroepigenetic markers.

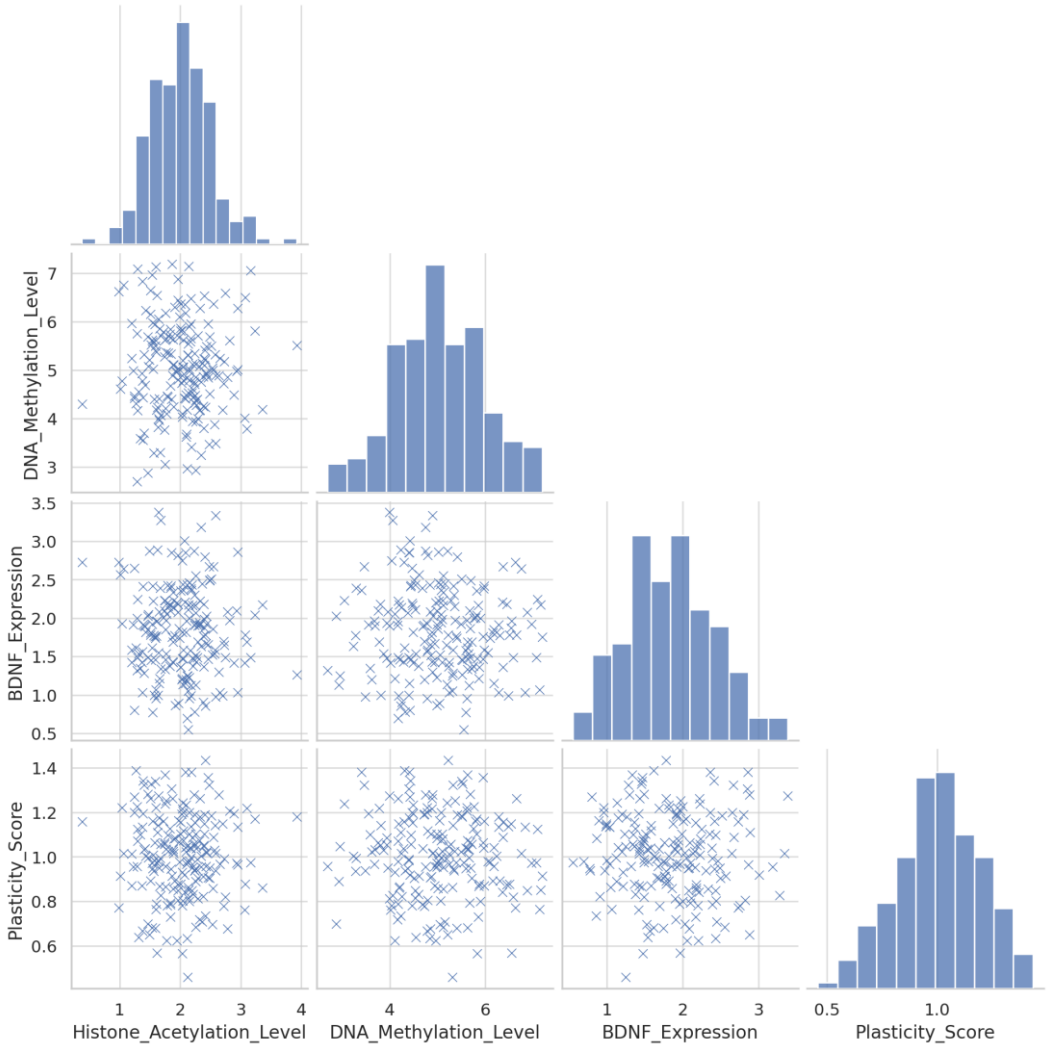


Figure 6. Fig6 pairplot

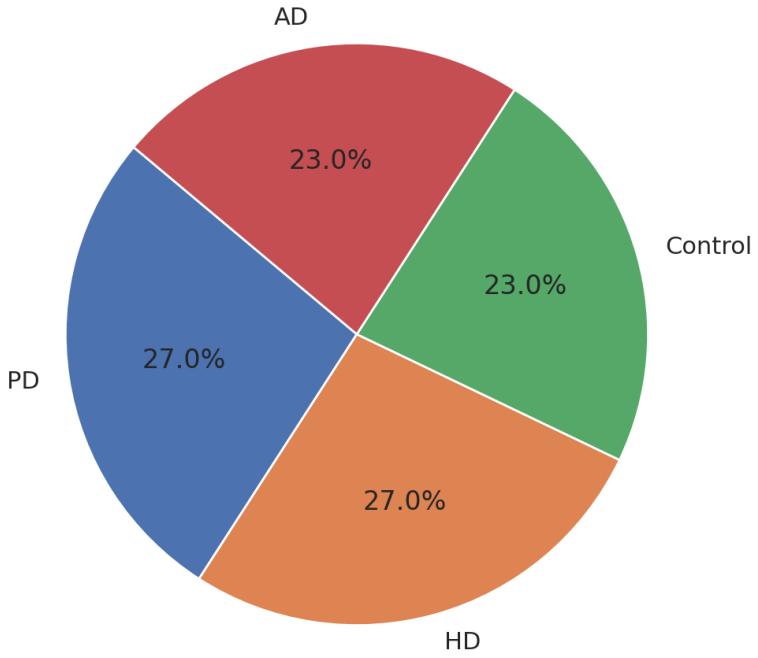


Figure 7. Fig7 pie group distribution

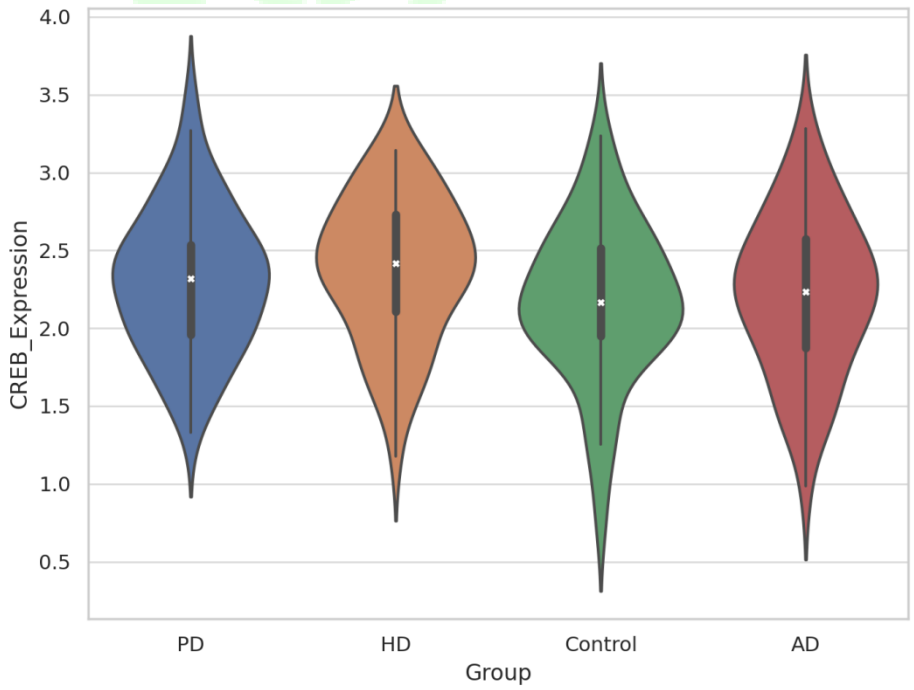


Figure 8. Fig8 violin creb expression

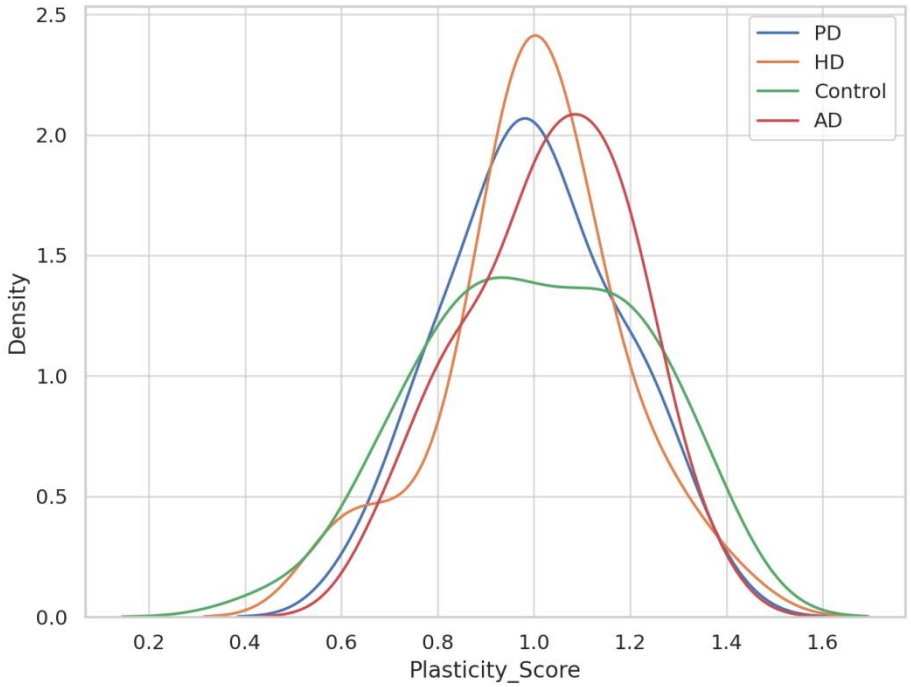


Figure 9. Fig9 kde plasticity

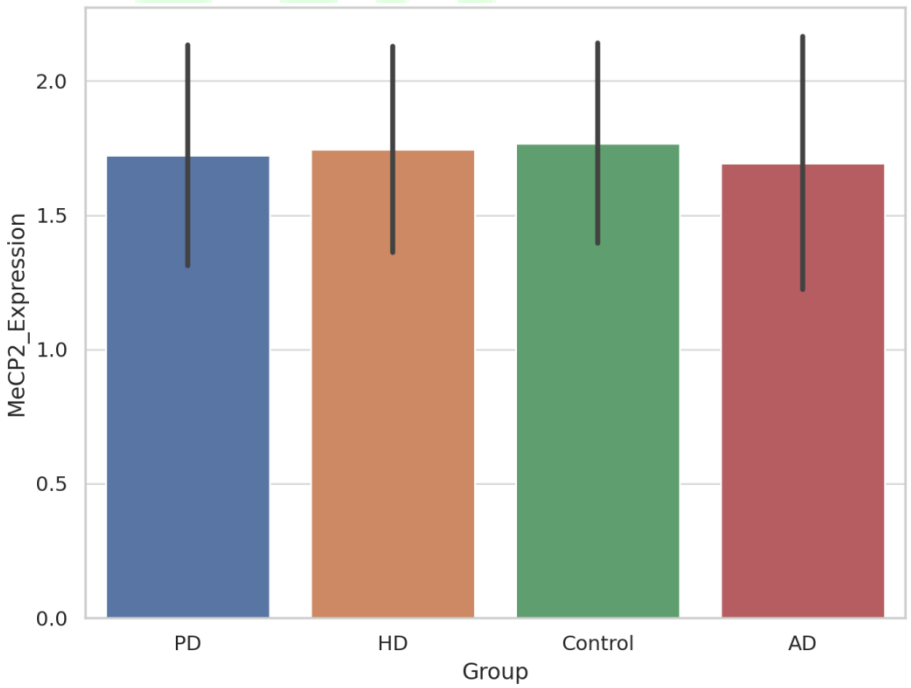


Figure 10. Fig10 mecp2 bar

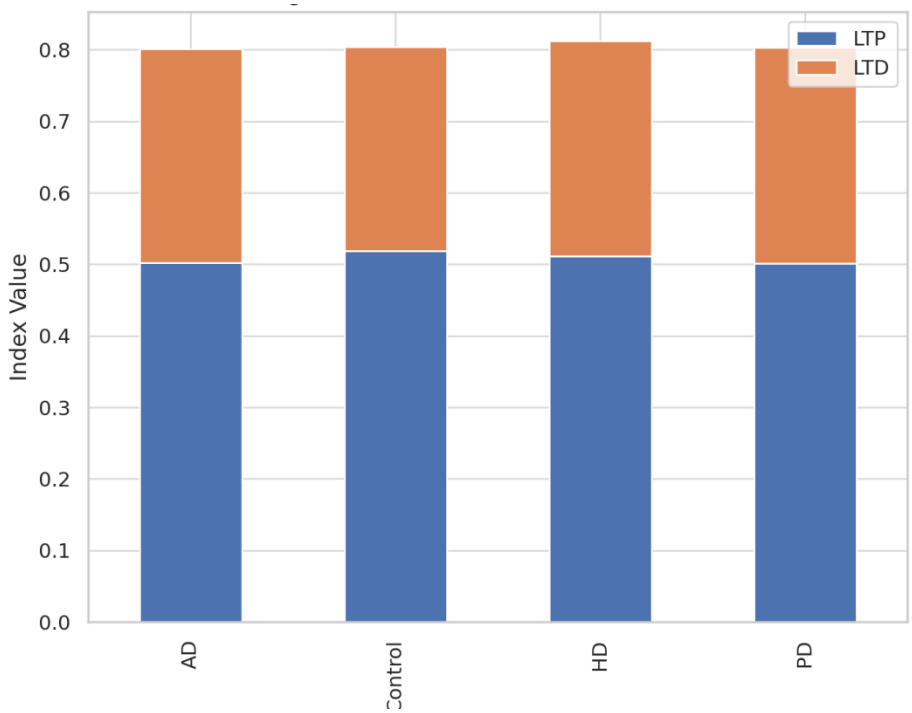


Figure 11. Fig11 stacked ltp ltd

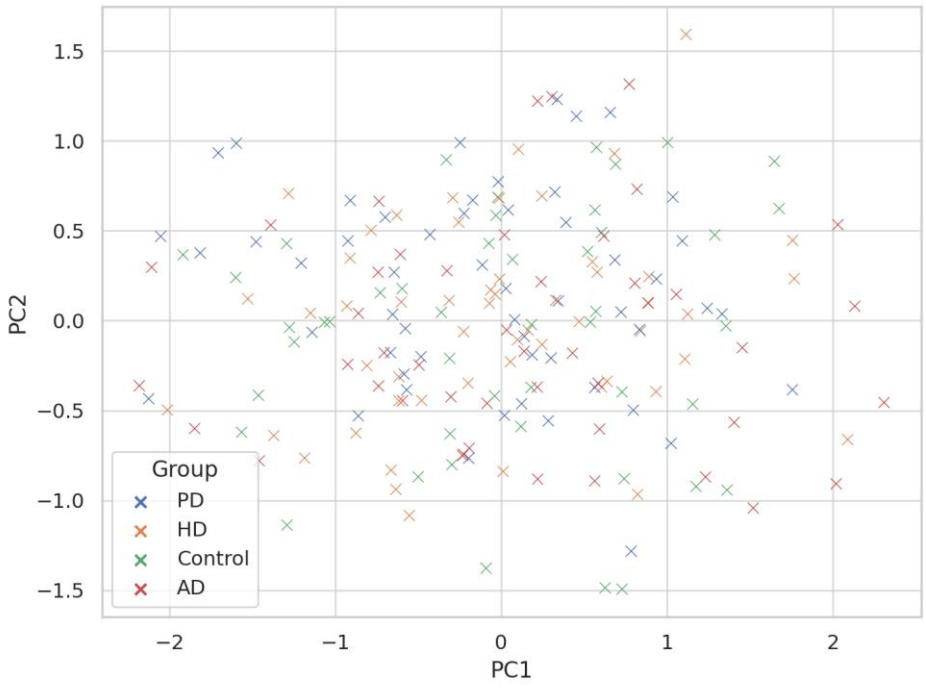


Figure 12. Fig12 pca

All these findings are corroborative of the view that some neuroepigenetic modifications, in particular those effecting HDACs, DNA methylation, and transcriptional regulators, such as BDNF or CREB, are tightly related to the issues of synaptic plasticity revealed in neurodegenerative diseases models.

DISCUSSION

In auditory cortex, the rehabilitation following noise trauma involves alteration of the functioning of various types of inhibitory interneurons. This is indicated by the fact that cortical adaptation is very complex because excitatory principal neurons, as well as some inhibitory neurons, recover sound-evoked activity (Kumar et al., 2023). Cortical sensory representations are requested to enhance mature cortical functioning through operant perceptual learning and passive exposure to sound (Thomas et al., 2020). It indicates that auditory cortex can adapt and repair itself although assistance can be required to ensure that plasticity results in positive outcomes (Thomas et al., 2020) (Schneider et al., 2022). Listenings In critical periods of growth, more sounding settings may alter the auditory cortex permanently, simplifying the processing and recognizing of auditory stimulates in busy locations and altering the shape of neurons (Pysanenko et al., 2021) (Homma et al., 2020). The findings indicate that individualized passive sounds exposures can potentially enhance slightly some adults in the perceptual abilities (Thomas et al., 2020). It is also significant regarding the hearing loss, which could be treated with the help of hearing aids or cochlear implants, to determine the impact of the changes in the brain caused by the development of the dementia in the hearing sense (Griffiths et al., 2020). However, with restored hearing through cochlear implants visual language may in some cases prove beneficial or detrimental to speech processing. It indicates that the topic on cross-modal reorganization and its influence on cognitive functioning still requires further investigation (Zhang et al., 2021). The capacity of the auditory cortex to influence the activity of subcortical auditory structures demonstrates the necessity of finding out more about the influence of cortical projections on the work of thalamus and inferior collis in the context of cochlear implants (Souffi et al., 2021). Hearing aids could even begin to soften the brain, and there is still little knowledge of how the auditory system is accommodated to new sounds (Karawani et al., 2022). Such shift may lead to the increased sensitivity and reduced adaptation to background noise of the brain and be associated with issues with perception (Resnik & Polley, 2021)Further studies are required to discover whether individuals with hearing issues can develop matured Cortical Auditory Evoked Potentials beyond the significant age, despite receiving no assistance with hearing loss (Palaniswamy et al., 2022). The acquired deafness may lead to the permanent hearing loss and to the impairment of the hearing response of auditory cortex to stimulus, demonstrating the significance of seeking assistance with hearing issues as early as possible (Palaniswamy et al., 2022). As well, auditory temporal processing may be improved through rehabilitation and selective sound therapy, particularly in individuals born with sensorineural hearing loss (Dziorny et al., 2021). The sensory decline could also be dealt with the help of hearing aids, but they may not be able to address noisy speech comprehension entirely (Frei & Giroud, 2025). Such types of issues need new means to enhance the cognition and audio covering (Arora et al., 2023). Therefore, to make practical solutions, it is necessary to understand the extent to which hearing loss, tinnitus, and aging influence brain

activity within the central auditory system (Fuksa et al., 2022).

CONCLUSION

Further studies are required to discover whether individuals with hearing issues can develop matured Cortical Auditory Evoked Potentials beyond the significant age, despite receiving no assistance with hearing loss (Palaniswamy et al., 2022). The acquired deafness may lead to the permanent hearing loss and to the impairment of the hearing response of auditory cortex to stimulus, demonstrating the significance of seeking assistance with hearing issues as early as possible (Palaniswamy et al., 2022). As well, auditory temporal processing may be improved through rehabilitation and selective sound therapy, particularly in individuals born with sensorineural hearing loss (Dziorny et al., 2021). The sensory decline could also be dealt with the help of hearing aids, but they may not be able to address noisy speech comprehension entirely (Frei & Giroud, 2025). Such types of issues need new means to enhance the cognition and audio covering (Arora et al., 2023). Therefore, to make practical solutions, it is necessary to understand the extent to which hearing loss, tinnitus, and aging influence brain activity within the central auditory system (Fuksa et al., 2022).

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