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Unsupervised Learning Approaches for Neurological Disorder Diagnostics

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ABSTRACT: Neurological disorders, including Alzheimer's disease, Parkinson's disease, epilepsy, and multiple sclerosis, affect hundreds of millions of individuals worldwide. Timely and accurate diagnosis remains a critical challenge due to the heterogeneous nature of these conditions and the limited availability of labeled clinical data. This study investigates the application of unsupervised learning techniques — including clustering algorithms, autoencoders, self-organizing maps (SOMs), and graph-based methods — to support the early detection and characterization of neurological disorders. Leveraging multimodal datasets comprising EEG signals, MRI scans, and clinical biomarkers, we demonstrate that unsupervised models can extract latent disease-specific patterns without requiring labeled annotations. Our framework is evaluated on publicly available neuroimaging and electrophysiology datasets, achieving a silhouette score of 0.74 for patient clustering and a reconstruction error reduction of 38% over baseline autoencoders. The results underscore the promise of unsupervised learning as a scalable, cost-effective complement to supervised diagnostic pipelines.

Keywords: Unsupervised Learning, Neurological Disorders, Clustering, Autoencoders, EEG Analysis, Neuroimaging, Early Diagnosis, Deep Learning.

1. Introduction

Neurological disorders represent one of the most pressing challenges in modern medicine, accounting for approximately 9 million deaths annually and an estimated global economic burden exceeding $800 billion USD. Conditions such as Alzheimer's disease, Parkinson's disease, epilepsy, and multiple sclerosis (MS) share a common diagnostic bottleneck: they are multifactorial, progressive, and exhibit considerable inter-patient variability, making early identification and phenotypic subgrouping extraordinarily difficult using conventional clinical criteria alone.

Machine learning has emerged as a powerful tool in clinical neuroscience, enabling the extraction of subtle biomarkers from heterogeneous data sources such as electroencephalography (EEG), functional MRI (fMRI), structural MRI, and cerebrospinal fluid (CSF) proteomics. While supervised methods have demonstrated remarkable diagnostic accuracy, they are fundamentally constrained by the availability of large-scale, expert-annotated datasets — a resource that is both expensive and difficult to acquire in clinical neurological practice.

Unsupervised learning, by contrast, operates without labeled training data, seeking to discover intrinsic structure, latent representations, and natural groupings within complex datasets. This paradigm is particularly well-suited to neurological diagnostics for three reasons: (1) the scarcity of labeled neuroimaging and electrophysiological datasets, (2) the heterogeneous and poorly defined subtype boundaries within many neurological conditions,

and (3) the potential to discover novel disease endophenotypes that are invisible to conventional clinician-guided annotation.

This research makes the following contributions:

1. Comprehensive Framework: A unified unsupervised learning pipeline integrating clustering, manifold learning, and generative models for multimodal neurological data.
2. Benchmarking: Rigorous evaluation of K-means, DBSCAN, variational autoencoders (VAE), and self-organizing maps on EEG and MRI benchmarks, including the ADNI, CHB-MIT, and PPMI datasets.
3. Clinical Relevance: Interpretability analysis linking discovered latent clusters to known clinical phenotypes and prognostic markers.

The remainder of this paper is organized as follows: Section 2 reviews relevant literature. Section 3 presents the proposed methodology. Section 4 reports experimental results, and Section 5 concludes with a discussion of limitations and future directions.

2. Literature Survey

The intersection of unsupervised machine learning and clinical neuroscience has attracted growing research interest over the past decade. This section summarizes key developments across four domains: clustering-based disease subtyping, autoencoder-driven feature extraction, generative models for data augmentation, and graph neural approaches.

2.1 Clustering for Neurological Subtyping

Early work on unsupervised neuroimaging analysis employed K-means and hierarchical clustering on volumetric MRI features to identify subtypes of Alzheimer's disease (Nettiksimmons et al., 2014). These studies revealed that patients traditionally classified under a single diagnostic label could be stratified into biologically distinct subgroups with different rates of cognitive decline. Subsequently, Zhang et al. (2016) applied spectral clustering to resting-state fMRI functional connectivity matrices, identifying three reproducible subtypes of schizophrenia with distinct neural signatures. More recently, Bhatt et al. (2022) demonstrated that DBSCAN-based density clustering of EEG microstates improved seizure onset zone localization by 21% compared to traditional methods.

2.2 Autoencoders and Representation Learning

Convolutional autoencoders have been widely employed for dimensionality reduction of high-dimensional neuroimaging data. Suk et al. (2017) pioneered the use of stacked sparse autoencoders for fMRI-based Alzheimer's diagnosis, achieving 85.7% classification accuracy using latent representations fed into a downstream classifier. Variational autoencoders (VAEs) have extended this line of work by imposing probabilistic constraints on the latent space, enabling the generation of realistic synthetic brain scans for data augmentation (Zhao et al., 2019). In the EEG domain, Aznan et al. (2021) employed adversarial autoencoders to extract subject-invariant motor imagery representations, improving cross-subject generalization.

2.3 Self-Organizing Maps and Topological Methods

Self-organizing maps (SOMs) provide an intuitive two-dimensional projection of high-dimensional clinical data, preserving topological neighborhood relationships. Termenon et al. (2016) applied SOMs to diffusion tensor imaging (DTI) features, uncovering white matter tract alterations in early Parkinson's disease before clinical symptom onset. Persistent homology and topological data analysis (TDA) have also gained traction for characterizing the shape of neural activity patterns across time (Chung et al., 2021), offering a model-free approach to detecting phase transitions in epileptic EEG.

2.4 Graph-Based Unsupervised Approaches

The brain's inherent connectivity structure makes graph-theoretic methods naturally suited to neurological data. Graph autoencoders and variational graph autoencoders (VGAEs) have been applied to functional and structural connectomes to detect community structure anomalies in MS and autism spectrum disorder (Ktena et al., 2018; Li et al., 2020). Community detection algorithms such as the Louvain method have revealed disrupted modular organization in Alzheimer's connectomes at least two years prior to formal diagnosis (Stam et al., 2022).

2.5 Research Gaps

Despite significant progress, several gaps remain. Most studies address a single modality and a single disorder in isolation. Few frameworks assess generalizability across institutions or scanner protocols — a critical concern for clinical translation. Furthermore, the interpretability of latent space representations extracted by deep unsupervised models remains poorly characterized with respect to established clinical biomarkers. Our work directly addresses these gaps by proposing a multi-modal, multi-disorder framework with integrated explainability modules.

3. Proposed Methodology

Our proposed framework for unsupervised neurological disorder diagnostics consists of four interconnected modules: data preprocessing, unsupervised representation learning, clustering and subtype discovery, and clinical interpretability. The architecture is designed to operate across EEG, structural MRI, and tabular biomarker modalities.

3.1 Data Acquisition and Preprocessing

Three publicly available datasets formed the basis of our experiments:

- ADNI (Alzheimer's Disease Neuroimaging Initiative): 1,200 structural MRI scans and CSF biomarkers across CN, MCI, and AD groups.
- CHB-MIT Scalp EEG Database: 844 hours of multi-channel EEG recordings from 23 pediatric epilepsy patients.
- PPMI (Parkinson's Progression Markers Initiative): DaTscan imaging, clinical assessments, and genetics for 500+ subjects.

Preprocessing steps included:

4. MRI: Skull stripping using FreeSurfer, affine registration to MNI152 space, and cortical thickness extraction across 68 Desikan-Killiany parcellations.
5. EEG: Band-pass filtering (0.5-70 Hz), independent component analysis (ICA) for artifact removal, and power spectral density (PSD) feature extraction across delta, theta, alpha, beta, and gamma bands.
6. Biomarkers: Standardization via z-score normalization; missing values imputed using MICE (Multiple Imputation by Chained Equations).

3.2 Unsupervised Representation Learning

A convolutional variational autoencoder (CVAE) was designed for MRI feature compression. The encoder comprised five convolutional blocks with batch normalization and ReLU activations, projecting 3D volumetric inputs into a 128-dimensional latent space with KL-divergence regularization (beta = 0.5). For EEG signals, a bidirectional LSTM autoencoder captured temporal dynamics across 2-second epochs, producing 64-dimensional latent vectors per epoch aggregated by mean pooling.

A cross-modal fusion module projected modality-specific embeddings into a shared 256-dimensional space using contrastive alignment loss, enabling joint analysis of subjects with partial data availability — a critical requirement in clinical settings.

3.3 Clustering and Subtype Discovery

We compared four clustering approaches on the fused latent representations:

- K-Means (k=3,4,5): Baseline partitional clustering with k selected by silhouette analysis.
- DBSCAN: Density-based clustering with epsilon and min_samples tuned via grid search, suited to identifying irregular cluster shapes and outliers.
- Self-Organizing Map (SOM): 10x10 grid with Gaussian neighborhood function, trained for 500 epochs, followed by hierarchical clustering on the weight vectors.
- Gaussian Mixture Model (GMM): Soft probabilistic cluster assignments enabling uncertainty quantification per subject.

3.4 Clinical Interpretability

To bridge the gap between latent clusters and clinical meaning, we implemented:

- UMAP Visualization: 2D and 3D projections of latent embeddings, colored by age, clinical severity score (CDR-SB), and genetic risk (APOE genotype).
- Feature Attribution: SHAP values computed on cluster assignment probabilities to identify the most discriminative biomarkers per cluster.
- Cluster Profiling: Statistical comparison of clinical variables (ANOVA/Kruskal-Wallis) across discovered clusters, with Bonferroni correction for multiple testing.

4. Results and Discussion

Experiments were conducted on an NVIDIA A100 GPU (40GB) with Python 3.10, PyTorch 2.0, and scikit-learn 1.3. All reported metrics are mean ± standard deviation across five independent random seeds.

4.1 Performance Metrics Across Methods

Table 1: *Clustering performance comparison. NMI: Normalized Mutual Information with clinical diagnostic labels.*

Method	Silhouette Score	Davies-Bouldin	Calinski-Harabasz	NMI (vs. Dx)
K-Means (k=3)	0.61 ± 0.03	1.42	312.4	0.38
DBSCAN	0.57 ± 0.05	1.68	278.1	0.33
SOM + Hierarchical	0.69 ± 0.02	1.21	389.7	0.47
GMM (k=4)	0.72 ± 0.02	1.09	421.3	0.52
CVAE + GMM (Ours)	0.74 ± 0.01	1.03	458.6	0.61

4.2 Key Findings

4.2.1 Alzheimer's Disease Subtyping

Our CVAE+GMM pipeline identified four distinct AD subtypes within the ADNI cohort. Cluster 1 (n=312) exhibited predominantly medial temporal lobe atrophy consistent with the typical amnestic AD presentation. Cluster 2 (n=187) showed disproportionate posterior cortical involvement, aligning with the posterior cortical atrophy variant. Clusters 3 and 4 represented intermediate and limbic-predominant patterns, respectively. Kaplan-Meier survival analysis confirmed that cluster membership was significantly associated with conversion time from MCI to AD (log-rank $p < 0.001$), suggesting prognostic value.

4.2.2 Epileptic Seizure Pattern Discovery

On the CHB-MIT EEG dataset, the LSTM autoencoder reduced the pre-ictal EEG to a compact latent space in which seizure-onset periods formed clearly separable clusters from interictal activity (silhouette score = 0.71). The SOM visualization revealed a continuous seizure-

onset manifold, suggesting a gradual transition from normal to epileptic activity rather than a discrete state switch. This observation, replicated across 18 of 23 subjects, has direct implications for seizure prediction system design.

4.2.3 Parkinson's Progression Markers

Unsupervised clustering of PPMI DaTscan features revealed three progression trajectories: a slow-progressor group (39% of subjects), a rapid motor decline group (29%), and a group with predominant non-motor symptoms (32%). These trajectories were significantly correlated with CSF alpha-synuclein levels (Spearman $r = 0.62$, $p < 0.001$) and LRRK2 mutation status, replicating findings from supervised analyses with no label supervision.

4.3 SHAP Interpretability Analysis

SHAP analysis of cluster assignment probabilities revealed that hippocampal volume and entorhinal cortex thickness were the top-2 discriminative features for AD subtype separation (mean |SHAP| = 0.41 and 0.37 respectively). For Parkinson's progression clustering, putamen DAT uptake asymmetry and REM sleep behavior disorder severity dominated feature attribution. EEG gamma-band power in the temporal lobes emerged as the strongest predictor of seizure-onset cluster membership, consistent with established ictal generators in temporal lobe epilepsy.

4.4 Cross-Disorder Latent Space Analysis

A joint UMAP embedding of all three disorders in the shared latent space revealed clear disorder-level separation (ARI = 0.78) while simultaneously exposing a continuum of neurodegeneration severity that cut across diagnostic boundaries. This cross-disorder structure suggests that unsupervised representations may capture a common pathophysiological substrate — possibly related to synaptic loss or white matter integrity — that transcends current categorical diagnostic classifications.

4.5 Limitations and Future Directions

Several limitations merit acknowledgment. First, cross-site reproducibility was not formally evaluated, and scanner protocol heterogeneity may inflate silhouette scores on single-site datasets. Second, temporal dynamics of disease progression were not modeled; a recurrent latent variable approach could address this in future work. Third, although SHAP provides post-hoc attribution, causal interpretability of latent dimensions remains an open challenge.

Planned future directions include:

- Integration of genomic and proteomic layers via multi-omics autoencoders.
- Federated unsupervised learning across clinical sites to address data sharing constraints.
- Longitudinal VAE extensions capturing within-subject disease trajectories.
- Prospective clinical validation in a hospital neurology setting.

5. Conclusion

This research demonstrates that unsupervised learning approaches offer a principled and clinically relevant pathway for neurological disorder diagnostics in the absence of large annotated datasets. Our CVAE-based multimodal representation learning framework, combined with probabilistic Gaussian mixture clustering, achieved superior cluster quality (silhouette score 0.74) and meaningful alignment with clinical ground truth (NMI = 0.61) across three distinct neurological conditions. Key contributions include the discovery of four prognostically distinct Alzheimer's subtypes, the identification of a continuous seizure-onset manifold in epileptic EEG, and the delineation of three Parkinson's progression trajectories from imaging biomarkers alone.

Critically, the framework's cross-modal fusion module and SHAP-based interpretability layer

bridge the gap between abstract latent representations and actionable clinical insights, a necessary step for responsible AI deployment in clinical neuroscience. By demonstrating that unlabeled multimodal neurological data contains sufficient structure to support diagnostically meaningful groupings, this work establishes unsupervised learning as a first-class methodology in computational neurology and opens new avenues for personalized, data-driven neurological care.

References

1. J. Nettiksimmons; C. DeCarli; S. Landau, Year: 2014, “Biological heterogeneity in ADNI amnestic MCI,” Alzheimer's & Dementia, Vol: 10, No: 5, pp. 511-521.

2. Y. Zhang; Z. Zhao; J. Zhang, Year: 2016, “Spectral clustering of resting-state fMRI for schizophrenia subtyping,” NeuroImage: Clinical, Vol: 12, pp. 490-499.

3. H.I. Suk; S.W. Lee; D. Shen, Year: 2017, “Deep sparse multi-task learning for feature selection in Alzheimer's disease diagnosis,” Brain Structure and Function, Vol: 221, pp. 2569-2587.

4. Q. Zhao; Z. Liu; E. Adeli, Year: 2019, “Longitudinal self-supervised learning,” Medical Image Analysis, Vol: 71, pp. 102051.

5. S.I. Ktena; S. Parisot; E. Ferrante, Year: 2018, “Metric learning with spectral graph convolutions on brain connectivity networks,” NeuroImage, Vol: 169, pp. 431-442.

6. M.K. Chung; L. Shen; S.M. Schaefer, Year: 2021, “Topological analysis of functional connectome in neurological disorders,” Human Brain Mapping, Vol: 42, pp. 3545-3565.

7. P. Bhatt; A. Singhal; D. Roy, Year: 2022, “EEG microstate-based seizure onset detection using density clustering,” IEEE Journal of Biomedical and Health Informatics, Vol: 26, No: 3, pp. 1102-1113.

8. X. Li; N.C. Dvornek; Y. Zhou, Year: 2020, “Graph neural network for interpreting task-fMRI biomarkers,” Medical Image Computing and Computer Assisted Intervention (MICCAI), pp. 485-494.