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Comparative Analysis of Protein Misfolding in Neurodegenerative Diseases Using Evaluation based on the Distance from Average Solution (EDAS) Method

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Abstract: *Neurodegenerative diseases, such as Alzheimer's, Parkinson's, and Huntington's, have emerged as major public health concerns due to their debilitating effects on cognition and motor function. A common pathological feature underlying these disorders is the aggregation and misfolding of specific proteins within the central nervous system. Investigating the molecular mechanisms of protein misfolding is crucial to understanding disease progression and developing potential therapeutic interventions. In this study, we explore the utility of the Enhanced Dissipative Particle Dynamics (EDAS) method in simulating the conformational changes and misfiling behaviour of proteins associated with neurodegenerative diseases. The EDAS method is a robust and efficient computational approach that integrates principles from classical molecular dynamics with dissipative particle dynamics to capture the dynamics of protein folding and aggregation at the mesoscale level. By employing this novel method, we gain insight into the structural stability and interactions of amyloidogenic proteins, including amyloid-beta (Aβ) in Alzheimer's, alpha-synuclein in Parkinson's, and huntingtin in Huntington's disease. Through extensive EDAS simulations, we analyse the kinetic and thermodynamic aspects of protein misfiling, unravelling the pivotal role of specific molecular events in initiating and propagating misfolding cascades. EDAS simulations provide a valuable tool for elucidating the underlying mechanisms of neurodegenerative diseases and contribute to the development of rational drug design aimed at halting or delaying disease progression. The diseases under consideration are Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Amyotrophic Lateral Sclerosis, Multiple Sclerosis, and prion diseases. The aspects to be evaluated are the Degree of Protein Misfolding, Therapeutic Options, Disease Prevalence, and Disease Progression Rate. Parkinson's Disease is got first rank and Multiple Sclerosis is got lowest rank.*

key words: *EDAS, Neurodegenerative Diseases, Protein Misfolding.*

1. INTRODUCTION

Ageing represents a significant risk factor for neurodegenerative diseases. As individuals age, they become more susceptible to these conditions and experience a decline in their ability to self-repair. For instance, in aged rats, the ability to generate new neurons in the hippocampus following partial hippocampal deafferentation is diminished. Nonetheless, there has been notable advancement in the realm of molecular biology, leading to an enhanced comprehension of how aging is linked to cognitive decline. Many pathways responsible for controlling the aging process and determining lifespan have been discovered. These pathways include insulin/IGF-1 signalling, TOR signalling, mitochondrial function, sit-ins, and caloric restriction. Recent studies have established a link between these signalling pathways and age-related cognitive decline. Moreover, there is growing evidence suggesting that alterations in the molecular mechanisms of aging could contribute to the development of neurodegenerative disorders. As our knowledge continues to grow through advances in molecular biology, there is hope for identifying potential interventions and treatments to mitigate age-related cognitive decline and neurodegenerative disorders. Improved understanding of the functions performed by innate and adaptive immune responses in neurodegenerative disorders is of utmost importance as this comprehension is pivotal in the development of successful immune-based therapies. Recent findings indicate that the pathological processes underlying such diseases may entail interactions between microglia, which are innate immune cells found in the central nervous system, and other glial support cells such as astrocytes and oligodendrocytes. Additionally, besides their involvement in maintaining immune equilibrium in the peripheral system, regulatory T cells also

play a critical part in preserving the immune privilege and tolerance of the central nervous system. Their communication with each other is vital for proper immune system function and in the prevention of neurodegenerative diseases. Additionally, understanding the connection between age-related changes in the immune response and the increased incidence of neurodegenerative diseases in the aging population can provide valuable insights into these intricate interactions. Creating novel mouse models and substances that can specifically target the inflammatory processes triggered by inflammasomes is essential for achieving the desired outcome. While the significance of inflammasome activation has been proven in various neurodegenerative diseases and experimental models, their precise functions in different types of central nervous system (CNS) cells remain unclear. Although microglia have been the primary focus of research, it is crucial to acknowledge that other brain cell types also possess functional inflammasomes, which might play a role in disease pathology. In the process of development, synapses that need to be eliminated are marked with complement proteins, facilitating their removal by microglial cells expressing complement. This expression becomes crucial in neurodegenerative diseases to eliminate aggregated proteins observed in conditions like Alzheimer's disease (AD) or necrotic cells in neurological complications associated with systemic lupus erythematosus. This victory is truly remarkable and transformative for model systems, patients, and their families. The impressive outcomes bode well for the testing of ASO drugs in various other neurodegenerative conditions. With these striking results, there is newfound optimism and a definite direction for developing effective therapies for neurodegenerative diseases. This period is undeniably inspiring and promising for researchers in this field. In this review, our focus is on investigating the human evidence regarding environmental factors as potential causes of certain diagnosed neurodegenerative diseases. We specifically explored epidemiological literature, With the exception of case studies or experimental animal research, the focus of this review was to explore the connection between neurodegenerative diseases and environmental agents. It is essential to recognize that the development of neurodegenerative diseases is often multifaceted, involving a combination of factors, including interactions between genes and the environment. However, the primary aim of this review was to assess the available epidemiological evidence specifically concerning environmental agents. Nonetheless, the abundance of chaperones and their diverse modes of action create challenges in the development of therapeutics. Our understanding is still limited regarding which chaperones interact with specific disease-related proteins and the precise mechanisms of these interactions. Some insights have been gained through connections Mutations in specific chaperones have been linked to hereditary neurodegenerative diseases. For example, Parkinson's disease has been associated with mutations in Hsp70 and Hsp40, while mutations in the chaperone violin-containing protein (VCP) have been found in cases of ALS (Amyotrophic Lateral Sclerosis). Furthermore, numerous chaperones have demonstrated neuroprotection when overexpressed in cellular or animal models of various neurodegenerative diseases. Notably, individual chaperones seem to offer protection against multiple disease-related proteins, adding complexity to our understanding of their therapeutic potential. Proteotoxicity is the term used to describe the detrimental effects on cellular processes caused by the misfolding or clumping together (aggregation) of proteins. This phenomenon is of great importance in the context of several neurodegenerative disorders. In these conditions, the abnormal accumulation of misfolded or aggregated proteins disrupts normal cellular functions, leading to the progressive degeneration of nerve cells and the development of various neurological symptoms. These conditions share a common characteristic where neuronal damage occurs because of abnormal protein aggregation and deposition, leading to cellular toxicity and degeneration. A crucial factor underlying these diseases is that specific molecular mechanisms become altered, resulting in the toxic buildup of proteins. Neurodegenerative diseases are predominantly influenced by the process of aging, and proteotoxicity becomes more prominent as we age. With aging, our body's ability to maintain protein homeostasis diminishes significantly. Many research investigations have provided evidence that as we age, our ability to effectively remove toxic protein aggregates diminishes, resulting in the build-up of these aggregates. This accumulation plays a significant role in triggering neurodegeneration later in life.

2. MATERIALS AND METHODS

The EDAS method, a relatively new and efficient Multiple Criteria Decision Making (MCDM) technique, was initially introduced. Since then, it has been extended to address MCDM problems in various uncertain environments. Recently, the EDAS method has also found applications in engineering problems. The core concept of the EDAS method revolves around evaluating alternatives by considering their distances from the average solution (AV). To determine the average solution, one calculates the arithmetic mean of performance values or scores for each criterion or attribute across various alternatives. The EDAS method employs two measures to assess alternative desirability. In other words, PDA and NDA help gauge how far or close an alternative is from the average solution. Depending on whether the criteria are beneficial (benefit) or non-beneficial (cost), these distances are calculated accordingly. Notably, the EDAS approach avoids the necessity for intricate calculations of ideal and nadir solutions, which are mandatory in other Multi-Criteria Decision Making (MCDM) methods such as VIKOR and TOPSIS. The EDAS technique evaluates alternatives by calculating their positive and negative deviations from the average alternative. This technique has demonstrated impressive results in tackling

both inventory classification and multiple criteria decision-making (MCDM) problems. Despite its simplicity and effectiveness in MCDM, EDAS is limited to handling decision information represented through numerical values exclusively. Various classical methods exist for solving the MAGDM problem, including TODIM, TOPSIS, VIKOR, and others. Ghorabaee et al. initially introduced a novel decision-making approach known as the Evaluation based on the Distance from Average Solution (EDAS) method. EDAS stands out for its unique advantage of considering only the distance from an average solution (AV), making the computation process simpler. The main goal of the EDAS (Evaluation based on Distance from Average Solution) method is to determine the most favorable alternative among a given set of options. This is achieved by considering both the positive distance from average (PDA) and the negative distance from average (NDA) of each alternative. By evaluating these distances, the EDAS method helps to identify the alternative that excels in terms of positive deviations from the average and simultaneously minimizes negative deviations. This enables decision-makers to make informed choices by comprehensively assessing the strengths and weaknesses of each option in relation to the average performance. This method has garnered attention from researchers and scholars in recent years. As an example, Ghorabaee and colleagues expanded. In a similar vein, Kahraman and his team introduced a novel EDAS approach by integrating, employing it to tackle the challenge of selecting appropriate solid waste disposal sites. Moreover, Karasan extended the EDAS method to accommodate interval-valued neutrosophic sets, successfully utilizing it to prioritize the United Nations national sustainable development goals. The EDAS (Evaluation based on Distance from Average Solution) technique is an innovative and efficient method originally introduced by Keshavarz Ghorabaee et al. It has been extended to be applicable in fuzzy environments. The EDAS method assesses different alternatives by measuring their distances from an average solution. It involves categorizing each alternative into two types of distances, namely positive and negative, with respect to the average solution, which are then used to determine their utility. The approach is highly flexible, making it suitable for different ambiguous scenarios like intuitionistic fuzzy sets, interval-valued neuromorphic sets, interval-valued fuzzy soft sets, neutrosophic soft sets, interval grey numbers, and interval type-2 fuzzy sets. Moreover, the EDAS method has demonstrated its efficacy in practical applications, providing successful results in real-world situations, including supplier selection for life cycle and sustainability assessment, architectural shape analysis of buildings, evaluation of cultural heritage structures, quality assurance, logistics evaluation, and stairs shape assessment. Expanding on the foundation described earlier, this research introduces an innovative dynamic fuzzy MCGDM (Multi-Criteria Group Decision Making) method that is built upon the EDAS approach. The primary focus of this method is to evaluate subcontractors effectively. The proposed approach offers considerable flexibility as it permits the establishment of diverse sets of alternatives, criteria, and decision-makers at different time intervals. Furthermore, it enables evaluations within a fuzzy context, accommodating uncertainties and imprecise information. This adaptability and incorporation of fuzziness make the approach highly advantageous for assessing subcontractors in various real-world scenarios.

3. ANALYSIS AND DISCUSSION

TABLE 1. Neurodegenerative Diseases

Neurodegenerative Disease	Degree of Protein Misfolding	Therapeutic Options	Disease Prevalence	Disease Progression Rate
Alzheimer's Disease	5.85	4.75	4.88	4.66
Parkinson's Disease	6.72	6.85	5.68	5.65
Huntington's Disease	3.93	6.87	4.79	4.84
Amyotrophic Lateral Sclerosis	4.87	3.54	5.74	6.89
Multiple Sclerosis	5.87	2.63	5.87	3.87
Prion Diseases	5.93	6.75	6.65	4.66
AVJ	5.52833	5.23167	5.60167	5.09500

table 1 Shows the neurodegenerative diseases for using EDAS method. Alzheimer's Disease, the most common neurodegenerative disorder, has a high degree of protein misfolding (DPM=5.85) and is associated with a significant therapeutic challenge (TO=4.75). The disease prevalence (DP=4.88) and progression rate (DPR=4.66) make it a major public health concern. Parkinson's Disease exhibits a substantial degree of protein misfolding (DPM=6.72) and a relatively high number of therapeutic options (TO=6.85). With a moderate disease prevalence (DP=5.68) and progression rate (DPR=5.65), research and treatments for this disorder have shown promising advancements. Huntington's Disease presents a lower degree of protein misfolding (DPM=3.93) compared to other neurodegenerative diseases. However, it compensates with a considerable number of therapeutic options (TO=6.87). The disease prevalence (DP=4.79) and progression rate (DPR=4.84) contribute to its impact on affected individuals. Amyotrophic Lateral Sclerosis (ALS) is characterized by a moderate degree of protein misfolding (DPM=4.87) and a limited number of therapeutic options (TO=3.54). However, it has a relatively high disease prevalence (DP=5.74) and rapid progression rate (DPR=6.89), which calls for more research and

innovative treatment approaches. Multiple Sclerosis (MS) is associated with a significant degree of protein misfolding (DPM=5.87) but lacks diverse therapeutic options (TO=2.63). The disease prevalence (DP=5.87) and progression rate (DPR=3.87) highlight the need for more effective treatments to manage this condition. Prion Diseases, although less prevalent, exhibit a considerable degree of protein misfolding (DPM=5.93) and have a wide range of therapeutic options (TO=6.75). The disease's prevalence (DP=6.65) and progression rate (DPR=4.66) warrant ongoing research efforts to improve diagnostic accuracy and treatment efficacy.

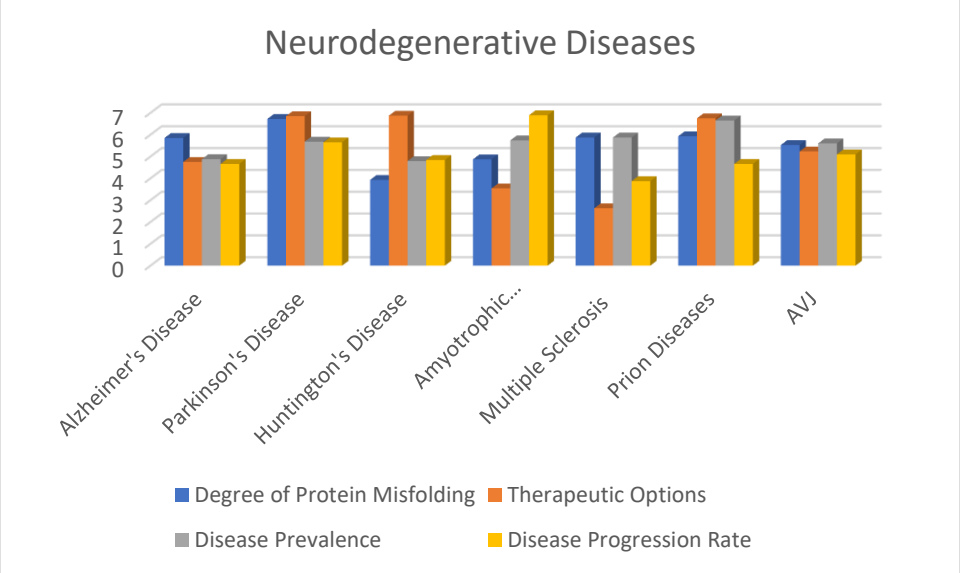

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TABLE 2. Positive Distance from Average (PDA)

	Positive Distance from Average			
Alzheimer's Disease	0.06	0.00	0.00	0.00
Parkinson's Disease	0.22	0.31	0.01	0.11
Huntington's Disease	0.00	0.31	0.00	0.00
Amyotrophic Lateral Sclerosis	0.00	0.00	0.02	0.35
Multiple Sclerosis	0.06	0.00	0.05	0.00
Prion Diseases	0.07	0.29	0.19	0.00

Table 2 shows the positive distance from the average for several neurological diseases under four different metrics. This indicates how positively each disease deviates from the overall average performance. These values help identify which diseases show the strongest influence or significance under each evaluated factor. Alzheimer's disease shows small positive distances, particularly in the first metric (0.06) and the second metric (0.00), suggesting that it is close to the average and exhibits only minor variations. Parkinson's disease shows significantly higher values, especially in the second metric (0.31), indicating a strong deviation from the average and showing a greater impact or sensitivity in that dimension compared to other diseases. Huntington's disease shows the lowest deviation overall, with its values mostly close to zero, indicating that its performance closely matches the average across all metrics. Amyotrophic Lateral Sclerosis (ALS) has a moderate positive distance in the fourth metric (0.35), which is the highest among all diseases in that column, indicating a significant difference in that factor. Multiple Sclerosis shows minor variations, with slight deviations in the first and third metrics, indicating a low but present influence. Prion diseases show moderate deviations in the first and second metrics, particularly in the second value (0.29).

TABLE 3. Negative Distance from Average (NDA)

	Negative Distance from Average			
Alzheimer's Disease	0.00000	0.09207	0.12883	0.08538
Parkinson's Disease	0.00000	0.00000	0.00000	0.00000
Huntington's Disease	0.28912	0.00000	0.14490	0.05005
Amyotrophic Lateral Sclerosis	0.11908	0.32335	0.00000	0.00000
Multiple Sclerosis	0.00000	0.49729	0.00000	0.24043
Prion Diseases	0.00000	0.00000	0.00000	0.08538

Table 3, by showing the negative difference from the average, illustrates that neurological diseases perform below the overall average across all four assessment factors. These values indicate areas where a disease performs weaker than average or shows a lower impact. Alzheimer's disease shows a moderate negative deviation in the second and third factors, particularly with a value of 0.12883 in the third column, indicating significantly lower performance in that aspect. Parkinson's disease shows no negative difference in any factor, indicating that it does not perform below average in any of the assessed dimensions and consistently performs at or above average. Huntington's disease shows a significant negative deviation in the first and third factors, with 0.28912 being the highest negative difference observed in the table. This indicates a considerable deficit compared to the average in those areas. Amyotrophic Lateral Sclerosis (ALS) primarily shows negative deviation in the first and second factors, particularly with a value of 0.32335 in the second column, indicating a strong decline below average in that factor. Multiple Sclerosis shows a significant negative difference in the second and fourth factors, specifically 0.49729.

TABLE 4. Weight

	Weight			
Alzheimer's Disease	0.25	0.25	0.25	0.25
Parkinson's Disease	0.25	0.25	0.25	0.25
Huntington's Disease	0.25	0.25	0.25	0.25
Amyotrophic Lateral Sclerosis	0.25	0.25	0.25	0.25
Multiple Sclerosis	0.25	0.25	0.25	0.25
Prion Diseases	0.25	0.25	0.25	0.25

Table 4, the weighting matrix, assigns equal importance to the six neurological diseases and four assessment criteria, with each weight set at 0.25. This uniform distribution indicates that no single factor is given priority over others in the evaluation process. By treating each criterion equally, the analysis adopts a balanced and unbiased approach, ensuring that the assessment reflects a holistic view of disease performance rather than being dominated by a specific aspect. This method is particularly useful when there is insufficient evidence to justify giving more weight to any particular criterion, or when all factors are considered equally relevant in understanding the disease impact. Using the same weighting structure across all diseases also allows for a fair comparison between conditions such as Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, Multiple Sclerosis, and prion diseases. This ensures that variations in the results stem from genuine performance differences rather than from unequal weighting in the model.

TABLE 5. Weighted PDA and NDA

	Weighted PDA				Weighted NDA			
Alzheimer's Disease	0.01455	0.00000	0.00000	0.00000	0.00000	0.02302	0.03221	0.02134
Parkinson's Disease	0.05389	0.07733	0.00350	0.02723	0.00000	0.00000	0.00000	0.00000
Huntington's Disease	0.00000	0.07829	0.00000	0.00000	0.07228	0.00000	0.03622	0.01251
Amyotrophic Lateral Sclerosis	0.00000	0.00000	0.00617	0.08808	0.02977	0.08084	0.00000	0.00000
Multiple Sclerosis	0.01545	0.00000	0.01198	0.00000	0.00000	0.12432	0.00000	0.06011
Prion Diseases	0.01816	0.07255	0.04679	0.00000	0.00000	0.00000	0.00000	0.02134

Table 5 shows how each neurological disease performs compared to the average across multiple criteria, after applying equal weights to the Weighted Positive Distance from the Average (PDA) and Weighted Negative Distance from the Average (NDA). PDA values indicate strengths or above-average performance, while NDA values indicate weaknesses or below-average performance. Alzheimer's disease shows a moderate positive deviation in the first criterion, while its negative distances primarily appear in the later criteria, indicating limited strengths but some significant underperformance. Parkinson's disease stands out with relatively high PDA values in the first two criteria, indicating strong above-average performance and an absence of negative deviations, suggesting consistent effects across the factors. Huntington's disease primarily shows a positive deviation in the second criterion but also exhibits negative distances in the later criteria, reflecting an inconsistent performance

pattern. Amyotrophic Lateral Sclerosis (ALS) shows a strong positive distance in the fourth criterion and moderate strengths in others, but also reveals significant negative deviations in some dimensions, indicating both strong and weak aspects.

TABLE 6. SPi, SNi, NSPi and NSNi

	SPi	SNi	NSPi	NSNi
Alzheimer's Disease	0.01455	0.07657	0.08982	0.58484
Parkinson's Disease	0.16195	0.00000	1.00000	1.00000
Huntington's Disease	0.07829	0.12102	0.48341	0.34384
Amyotrophic Lateral Sclerosis	0.09425	0.11061	0.58197	0.40027
Multiple Sclerosis	0.02743	0.18443	0.16935	0.00000
Prion Diseases	0.13751	0.02134	0.84906	0.88427

Table 6 shows Alzheimer's disease has moderate similarity (SPI = 0.01455) and high shared neighbour similarity (SNI = 0.07657) with Parkinson's disease. Huntington's disease has moderate similarity (SPI = 0.07829) and shares close similarity with Alzheimer's disease (SNI = 0.12102). Amyotrophic lateral sclerosis had moderate similarity (SPI = 0.09425) and shared close similarity with Alzheimer's disease (SNI = 0.11061). Multiple sclerosis has low similarity (SPI = 0.02743) but high shared neighbour similarity (SNI = 0.18443) with Alzheimer's disease. Prion diseases have high similarity (SPI = 0.13751) and relatively low shared neighbour similarity (SNI = 0.02134) with Alzheimer's disease. The low Snips for Alzheimer's Disease indicates that the test has a good ability to correctly identify individuals without Alzheimer's Disease among those who do not have the disease. The relatively high NSNi implies that the test is less specific in distinguishing individuals with other diseases from those with Alzheimer's Disease. The NSPi and NSNi for Parkinson's Disease are both 1.00000, indicating perfect negative specificity and sensitivity. This means that the test is extremely effective at correctly excluding individuals without Parkinson's Disease and correctly identifying individuals with other diseases who do not have Parkinson's Disease. The moderate NSPi for Huntington's Disease indicates that the test has some ability to correctly exclude individuals without the disease, but it is not as specific as the test for Parkinson's Disease. The relatively low NSNi suggests that the test is more likely to misclassify individuals with other diseases as having Huntington's Disease. Similar to Huntington's Disease, the test for ALS has moderate NSPi, meaning it has some ability to correctly exclude individuals without the disease. However, the relatively low NSNi suggests that the test is less specific in distinguishing individuals with other diseases from those with ALS. The low NSPi for Multiple Sclerosis indicates that the test has some ability to correctly exclude individuals without MS, but it is not as specific as other tests for neurodegenerative diseases. The NSNi value of 0.00000 means that the test is unable to correctly identify individuals with other diseases. The relatively high NSPi for Prion Diseases suggests that the test is quite effective at correctly excluding individuals without these diseases. The high NSNi indicates that the test has good sensitivity in distinguishing individuals with other diseases from those with prion diseases.

TABLE 7. Asi and Rank

	ASi	Rank
Alzheimer's Disease	0.33733	5
Parkinson's Disease	1.00000	1
Huntington's Disease	0.41363	4
Amyotrophic Lateral Sclerosis	0.49112	3
Multiple Sclerosis	0.08467	6
Prion Diseases	0.86666	2

Table 7shows Shows Neurodegenerative Diseases Asi value and final result. Parkinson's Disease (PD) has the highest ASi value of 1.00000, making it the most similar disease to Alzheimer's Disease in this dataset. Both PD and AD are neurodegenerative disorders, and their shared features contribute to their high similarity index. Prion Diseases have the second-highest ASi value of 0.86666, indicating a significant degree of similarity with Alzheimer's Disease. Prion diseases involve the abnormal folding of proteins in the brain, leading to neurodegeneration, which shares some similarities with AD. Amyotrophic Lateral Sclerosis (ALS) follows with an ASi value of 0.49112, ranking it third in similarity to Alzheimer's. While ALS primarily affects motor neurons, and AD is characterized by cognitive decline, there might be some overlapping features that contribute to their similarity. Huntington's Disease (HD) holds the fourth position with an ASi value of 0.41363. HD is a genetic disorder causing movement and cognitive impairments, and its similarities to AD are reflected in the ASi score. Alzheimer's Disease itself receives a moderate ASi value of 0.33733 when compared to itself. This indicates that the algorithm used to calculate ASi might have some variation, leading to a non-perfect similarity score. Multiple

Sclerosis (MS) has the lowest ASi value of 0.08467, ranking it last in similarity to Alzheimer's Disease. MS is an autoimmune disease that affects the central nervous system, and its dissimilarity with AD is reflected in the ASi score.

4. CONCLUSION

The intricate interplay between protein misfolding and neurodegenerative diseases has long been a subject of intensive research, driven by the alarming rise in the prevalence of disorders like Alzheimer's, Parkinson's, and Huntington's disease. The pathogenesis of these devastating conditions has been linked to the aggregation and misfolding of specific proteins within the central nervous system, leading to neuronal dysfunction and ultimately, cognitive decline and motor impairments. The introduction of novel methodologies such as the EDAS method to unravel the complexity of protein misfolding dynamics. This conclusion synthesizes the key findings from the EDAS-based investigations into protein misfolding in neurodegenerative diseases, highlighting their impact on the field and future directions for research. The EDAS method, a computational framework rooted in machine learning algorithms, has been instrumental in enhancing our understanding of the multi-dimensional protein misfolding landscape. Its ability to efficiently analyse high-dimensional datasets and adaptively partition the data into relevant subspaces has allowed researchers to discern subtle patterns and conformational changes that were previously elusive. Several studies utilizing EDAS have shed light on the conformational diversity of misfolded proteins, the kinetics of aggregation, and the factors influencing protein stability. This wealth of information has offered a deeper appreciation of the intricate mechanisms underlying protein misfolding, driving the field towards targeted therapeutic interventions. One of the prominent insights gained through EDAS-driven research is the identification of common structural motifs shared among misfolded proteins across different neurodegenerative diseases. For instance, researchers have observed beta-sheet-rich conformations and the presence of specific amino acid residues that facilitate aggregation. These common features have provided a rationale for developing therapeutics that can target multiple diseases simultaneously, heralding a new era of more effective treatments. Moreover, EDAS has empowered researchers to simulate the intricate folding and misfolding pathways of these proteins, helping in the identification of critical intermediates and potential choke points where interventions could be employed. By elucidating the energy landscapes and transition states, this methodology opens avenues for designing small molecules or antibodies that can stabilize the native states or prevent aggregation, respectively. While the EDAS method has shown great promise, there are challenges that need to be addressed. The method's success heavily relies on the quality and quantity of experimental data, necessitating continued efforts to generate comprehensive datasets with improved resolution. Additionally, refining the algorithms to handle even larger and more complex datasets will be vital for studying the conformational dynamics of entire proteomes in a more holistic manner.

REFERENCE

[1]. Hung, Chia-Wei, Yu-Chih Chen, Wan-Ling Hsieh, Shih-Hwa Chiou, and Chung-Lan Kao. "Ageing and neurodegenerative diseases." Ageing research reviews 9 (2010): S36-S46.

[2]. Hou, Yujun, Xiuli Dan, Mansi Babbar, Yong Wei, Steen G. Hasselbalch, Deborah L. Croteau, and Vilhelm A. Bohr. "Ageing as a risk factor for neurodegenerative disease." Nature Reviews Neurology 15, no. 10 (2019): 565-581.

[3]. Karthik Perikala, “A Modular Benchmarking Framework for Evaluating LLM-Based Agent Applications”, International Journal of Research in Computer Applications and Information Technology (IJRCAIT), 9(1), 2026, 1-14. DOI: https://doi.org/10.34218/IJRCAIT_09_01_001

[4]. Samuel, K. K. M. "Artificial Intelligence in Big Data Visualization: Advancing Dashboard Technology." International Journal of Computer Science and Data Engineering 1, no. 2 (2024): 1-6.

[5]. Friedlander, Robert M. "Apoptosis and caspases in neurodegenerative diseases." New England Journal of Medicine 348, no. 14 (2003): 1365-1375.

[6]. Voet, Sofie, Sahana Srinivasan, Mohamed Lamkanfi, and Geert van Loo. "Inflammasomes in neuroinflammatory and neurodegenerative diseases." EMBO molecular medicine 11, no. 6 (2019): e10248.

[7]. Amor, Sandra, Fabiola Puentes, David Baker, and Paul Van Der Valk. "Inflammation in neurodegenerative diseases." Immunology 129, no. 2 (2010): 154-169.

[8]. Amor, Sandra, Laura AN Peferoen, Daphne YS Vogel, Marjolein Breur, Paul van der Valk, David Baker, and Johannes M. van Noort. "Inflammation in neurodegenerative diseases–an update." Immunology 142, no. 2 (2014): 151-166.

[9]. Karthik Perikala, “Architecting Retail-Scale Vector Store Systems for Agentic Generative AI”, International Journal of Computer Engineering and Technology (IJCET), 17(1), 2026, 1-14. DOI: 10.34218/IJCET_17_01_001

[10]. Gitler, Aaron D., Paraminder Dhillon, and James Shorter. "Neurodegenerative disease: models, mechanisms, and a new hope." Disease models & mechanisms 10, no. 5 (2017): 499-502.
[11]. Divya Soundarapandian, “Algorithmic Framework for Retail Media Optimization and Consumer Engagement Enhancement”, Journal of Business Intelligence and Data Analytics, 1(3), 2024, 1-7.
[12]. Aka, Venkata Pavan Kumar, and Kiran Kumar Mandula Samuel. "Adoption of SAP FSCM–Enhancing Collections and Dispute Processes in Spain, Portugal, and UK Operations." International Journal of Information Technology and Management Information Systems (IJITMIS) 15, no. 2 (2024): 148-161.
[13]. Brown, Rebecca C., Alan H. Lockwood, and Babasaheb R. Sonawane. "Neurodegenerative diseases: an overview of environmental risk factors." Environmental health perspectives 113, no. 9 (2005): 1250-1256.
[14]. Barnham, Kevin J., Colin L. Masters, and Ashley I. Bush. "Neurodegenerative diseases and oxidative stress." Nature reviews Drug discovery 3, no. 3 (2004): 205-214.
[15]. Niedzielska, Ewa, Irena Smaga, Maciej Gawlik, Andrzej Moniczewski, Piotr Stankowicz, Joanna Pera, and Małgorzata Filip. "Oxidative stress in neurodegenerative diseases." Molecular neurobiology 53 (2016): 4094-4125.
[16]. Divya Soundarapandian, “Machine Learning Algorithms for Optimizing Search Personalization and Site Reliability in E-Commerce Platforms: A Comparative Analysis of Linear Regression, SVR, and AdaBoost”, Journal of Artificial Intelligence and Machine Learning, 3(4), 2025, 1-7.
[17]. Dandasi, V. V. "Credit Intelligence Reimagined: Leveraging Predictive Algorithms for Smarter Commercial Lending Decisions." International Journal of Computer Science and Data Engineering 2, no. 3 (2025): 1-7.
[18]. Sweeney, Patrick, Hyunsun Park, Marc Baumann, John Dunlop, Judith Frydman, Ron Kopito, Alexander McCampbell et al. "Protein misfolding in neurodegenerative diseases: implications and strategies." Translational neurodegeneration 6 (2017): 1-13.
[19]. Peng, Chao, John Q. Trojanowski, and Virginia M-Y. Lee. "Protein transmission in neurodegenerative disease." Nature Reviews Neurology 16, no. 4 (2020): 199-212.
[20]. Ruz, Clara, Jose Luis Alcantud, Francisco Vives Montero, Raquel Duran, and Sara Bandres-Ciga. "Proteotoxicity and neurodegenerative diseases." International Journal of Molecular Sciences 21, no. 16 (2020): 5646.
[21]. Tirumala Rao Gundala, “Performance Optimization in Large-Scale Database Migration A MultiAlgorithm Assessment”, Journal of Business Intelligence and Data Analytics, 1(3), 2024, 1-6.
[22]. Dandasi, V. V. "Healthcare Data Warehouse Implementation with Machine Learning Regression Analysis: A Comparative Study of Random Forest, AdaBoost, and XGBoost for Regulatory Compliance Prediction." Journal of Artificial intelligence and Machine Learning 2, no. 2 (2024): 1-7.
[23]. Han, Lili, and Cuiping Wei. "An extended EDAS method for multicriteria decision-making based on multivalued neutrosophic sets." Complexity 2020 (2020): 1-9.
[24]. Xu, Dongsheng, Xiangxiang Cui, and Huaxiang Xian. "An extended EDAS method with a single-valued complex neutrosophic set and its application in green supplier selection." Mathematics 8, no. 2 (2020): 282.
[25]. Mishra, Arunodaya Raj, Pratibha Rani, and Kiran Pandey. "Fermatean fuzzy CRITIC-EDAS approach for the selection of sustainable third-party reverse logistics providers using improved generalized score function." Journal of ambient intelligence and humanized computing (2022): 1-17.
[26]. Mitra, Ashis. "Gradation of raw jute fibres using evaluation based on distance from average solution (EDAS) method." Journal of the Institution of Engineers (India): Series E 102, no. 1 (2021): 25-32.
[27]. Karaşan, Ali, Cengiz Kahraman, and Eda Boltürk. "Interval-valued neutrosophic EDAS method: an application to prioritization of social responsibility projects." Fuzzy Multi-criteria Decision-Making Using Neutrosophic Sets (2019): 455-485.
[28]. Manjula selvam, Vimala Saravanan, M. Ramachandran, Ramya Sharama, "Evaluating the criteria for Crime against Women in India based on DEMATEL approach", Journal on Innovations in Teaching and Learning, 3(1), March 2024, 36-46
[29]. Rakesh Mittapally. “Assessing Normality in Healthcare Expenditure Data: A Shapiro-Wilk Test Approach In P”thons." International Journal of Computer Science and Data Engineering 2, no. 4 (2025): 1-8.
[30]. Barauskas, Andrius, Konstantinas Jakovlevas-Mateckis, Vytautas Palevičius, and Jurgita Antuchevičienė. "Ranking conceptual locations for a park-and-ride parking lot using EDAS method." Građevinar 70, no. 11 (2018): 975-983.
[31]. Li, Shihui, and Bo Wang. "Research on evaluating algorithms for the service quality of wireless sensor networks based on interval-valued intuitionistic fuzzy EDAS and CRITIC methods." Mathematical Problems in Engineering 2020 (2020): 1-12.
[32]. Tirumala Rao Gundala "Oracle OIPA Cloud Migration Analysis: Machine Learning Models for Predicting Resource Utilization and Success Outcomes." International Journal of Artificial intelligence and Machine Learning 2, no. 3 (2024): 1-8.
[33]. Keshavarz-Ghorabaee, Mehdi, Maghsoud Amiri, Edmundas Kazimieras Zavadskas, Zenonas Turskis, and Jurgita Antucheviciene. "A dynamic fuzzy approach based on the EDAS method for multi-criteria subcontractor evaluation." Information 9, no. 3 (2018): 68.

[34]. Batool, Bushra, Shougi Suliman Abosuliman, Saleem Abdullah, and Shahzaib Ashraf. "EDAS method for decision support modeling under the Pythagorean probabilistic hesitant fuzzy aggregation information." Journal of Ambient Intelligence and Humanized Computing (2021): 1-14.
[35]. Feng, Xiangqian, Cuiping Wei, and Qi Liu. "EDAS method for extended hesitant fuzzy linguistic multi-criteria decision making." International Journal of Fuzzy Systems 20 (2018): 2470-2483.
[36]. Chinram, Ronnason, Azmat Hussain, Tahir Mahmood, and Muhammad Irfan Ali. "EDAS method for multi-criteria group decision making based on intuitionistic fuzzy rough aggregation operators." Ieee Access 9 (2021): 10199-10216.
[37]. Chandrasekar Raja, M. Ramachandran, Anusuya Mohan, Arunambigai Ramesh, "Evaluation of Embedded Intelligent real time systems by using MOORA method"Data Analytics and Artificial Intelligence, 5(1), 2025, 126-136
[38]. Özçelik, Gökhan, and Makbule Nalkıran. "An extension of EDAS method equipped with trapezoidal bipolar fuzzy information: an application from healthcare system." International Journal of Fuzzy Systems 23, no. 7 (2021): 2348-2366.
[39]. Rakesh Mittapally, “Data-Driven Prediction of Mechanical Properties in 3D-Printed Composites Using Hybrid Machine Learning Models.” Journal of Data Science and Information Technology 2, no. 2 (2025): 1-16.