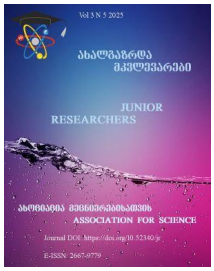
Junior researchers

ახალგაზრდა მკვლევარები

Vol. 3 Issue 5, 2025

https://doi.org/10.52340/jr.2025.03.05.12



Artificial Intelligence Integration with Advanced MRI Biomarkers for Early and Differential Diagnosis of HSV Encephalitis

Parvin Mozafari[1], Adiba Khan[2], Khalid Haddad[3], Anton Haddad[4], Sadaf Khanam[5]

1-Faculty of medicine, University of Georgia, Tbilisi, Georgia.

2- Faculty of medicine, University of Georgia, Tbilisi, Georgia.

3- Faculty of Medicine, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania.

4- New vision university, faculty medicine, Tbilisi, Georgia.

5- Tbilisi State Medical University, Faculty of Dentistry, Tbilisi, Georgia.

**Corresponding author: Parvin Mozafari1, Faculty of medicine, University of Georgia, Tbilisi, Georgia, Parvinmozaffari73@gmail.com, Phone number: +995-591096156

** ORCID: Parvin Mozafari: 0009-0002-8107-2390, Adiba Khan: 0009-0002-2690-1002, Khalid Haddad: 0009-0000-0181-4733, Anton Haddad: 0009-0003-3703-0238, Sadaf Khanam: 0009-0004-7416-4769.

Abstract

Herpes simplex virus of the brain (HSE) is a life-threatening neurological emergency which is characterized by high morbidity and mortality unless early diagnosed and treated. Recognition promptly is essential, because the mortality rate in untreated cases is about 70 percent whereas antiviral therapy decreases the death rate to 10-20 per cent in populations/patients treated and prevents long term neurological-cognitive sequelae. Developed magnetic resonance imaging (MRI) has been the key in the early detection of the HSE and the use of sequences like diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR), and T2-weighted imaging has been found to be of high sensitivity and specificity. The lesions tend to be restricted to medial temporal lobes and limbic structures although extratemporal and bihemispheric damages have been reported. These imaging biomarkers can distinguish other pathologies, like neoplasm and cerebro vascular event, and can be employed to distinguish between HSE and autoimmune encephalitis (AE), which can both share similar clinical and radiologic phenotypes. The most recent advances in artificial intelligence (AI), which include classical machine learning (CML) and deep learning (DL) have shown significant potential to increase diagnostic accuracy. The presence of AI in combination with multi-sequence MRI allows automatic lesion detection, increased pattern recognition, and better classification between HSE, AE, and gliomas. Imaging with clinical and laboratory data such as cerebral things of analysis, serological marker and patient demographics have shown a better performance in diagnosis compared to the diagnostic performance of experienced radiologists and could predict functional outcome and cognitive recovery. However, a few issues restrict the use of multicenter imaging, such as inconsistent

image schemes, small sample sizes, and technical demands of sophisticated imaging techniques like pseudo continuous arterial spin labeling (pCASL). Standardization of imaging workflows, larger multicenter and prospective validation studies must determine the reproducibility, generalization and clinical utility of imaging workflows. Synergistic use of high-tech MRI biomarkers with AI-related analytics is a perspective of early and differentiated diagnosis of HSE. These combined methods can help significantly improve patient outcomes and decrease the HSE-related burden of neurological morbidity because of timely antiviral intervention and individualized long-term care.

Keywords: Herpes Simplex Virus Encephalitis (HSE), Artificial Intelligence, Advanced MRI Biomarkers, Differential Diagnosis.

Introduction

Encephalitis can be defined as the inflammation of the brain's parenchyma, potentially accompanied by neurologic impairments (1). This pathology is responsible for the hospitalization of approximately 7 patients per 100,000 population per year in the United States (2). Encephalitis can generally be split, according to etiology, into infectious and autoimmune. Despite a comprehensive evaluation, 37-62% of patients presenting with encephalitis still end up with an idiopathic etiology (3). Out of the cases whose etiology is known, Viral ones are 20-50 percent of which herpes simplex encephalitis (HSE) is the most prevalent, responsible in 50-75% of cases of viral encephalitis (2). In adults, herpes simplex encephalitis (HSE) is caused in almost 90 percent of cases by herpes simplex virus type 1 (HSV-1), but in neonates, HSV-2 is the leading cause (4,5). The primary infection of HSV is usually acquired as a result of the breaches in the skin or mucous membranes. After entry, the virus infects the sensory neurons and establish latency in the ganglia. It is theorized that HSV has access to the central nervous system through hematogenous or retrograde transport along the olfactory or trigeminal nerves. Also, currently in contention is whether HSE is caused by primary infection or latent reactivation of HSV. It is also important to mention that HSV spread is prevalent in the group of people. General population, where HSV-1 seropositivity is estimated at 54% and HSV-2<|human|>general population, where HSV-1 seropositivity stands at 54% and HSV-2<|human|>general population, where HSV-1 seropositivity is estimated at 54% and HSV-2. Positivity of serum in 14-49-year-old Americans at 16% (1). HSE is a very severe brain infection with multiple complications, including hemorrhage, necrosis, and edema. The typically impacted areas of the brain are the medial temporal lobes and limbic areas (insular, cingulate, and inferolateral frontal cortices) (6). The symptoms of HSE develop over several days and usually include encephalopathy, fever, seizures, headaches, and focal neurological deficits. The main reasons for HSE patient admission to the hospital tend to be seizures, abnormal behavior, loss of consciousness, and disorientation (1).

If gone untreated, HSE has a critical mortality rate of roughly 70% with 97% of the survivors never returning to the same level of brain function. The standard first-line treatment is IV acyclovir (an antiviral drug) at a dose of 10 mg/kg q8h for 14-21 days (1). With treatment, the patient mortality rate

drastically reduces to about 10-20 and in spite of this, after infection, there will still be a large disability burden among the patients and other types of sequelae such as. Personality changes, behavioral changes, seizures, dysphasia, epilepsy and memory issues. (4) (6) (7).

HSE is severe and rapidly progressive, therefore, the healthcare provider needs to be highly alert and promptly diagnose and treat the disease to minimize morbidity, mortality and improve treatment efficacy. Diagnosis, which is essential to prompt treatment, is delayed or missed because of delays in brain imaging and overlapping of symptoms and results with other disorders, including autoimmune encephalitis (AIE) (5,8).

If encephalitis is confirmed, an essential test that should be performed in all patients is a lumbar puncture to measure the opening pressure, cell count, cell differential and a polymerase chain reaction (PCR) test that sought the presence of copies of herpes simplex viral DNA in the CSF (1). It is worth mentioning that a significant diagnostic pitfall for the HSV PCR test is the likelihood of a false-negative result, especially early on in the infection, due to insufficient copies. If suspicion is high, then the CSF HSV PCR test should be repeated within 3-7 days (1) (3). For other findings used to distinguish HSE from AIE, Tan et al. (8) found non-specific test trends like HSE patients having a higher occurrence rate of abnormal myocardial enzyme spectrum, increased incidence of thyroid dysfunction, higher positive rate of tumor markers, as well as higher number and protein content of CSF leukocytes. The study also found that lesion distribution varies significantly between HSE and AIE. In patients with HSE, lesions are typically found on a single lobe or as multiple asymmetrical lesions in the limbic system, most frequently in the medial temporal lobes as well as the insular, cingulate, and frontonasal cortex (8).

In a study, it was reported that for all the HSE patients tested, CT scan findings were abnormal for about half of all cases, whilst MRI scan findings were abnormal for nearly all cases (1). For early diagnostic brain imaging, CT scans struggle to differentiate between HSE and its look-alikes, while also being inadequate in sensitivity, thus cementing MRI scans as the gold standard diagnostic option. The most important MRI sequences used for HSE diagnosis are T2, fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) (5). In a recent study examining HSE patients, abnormal FLAIR hyperintensities were seen in nearly all, with findings like ≥3 lobe lesions (in 38.4%), bilateral damage (in 36.2%), and lesions limited to 1 hemisphere (in 61.6%). The same study also included findings for diffusion restriction on DWI, which contained hyperintensities in about half of all patients with findings like ≥3 lobe lesions (in 26.9%) and thalamic abnormalities (in 46.3%) (7). DWI results are exceptionally important for early diagnosis, as there is mounting evidence that diffusion restriction is one of the earliest neuroradiologic findings that can be seen in HSE, sometimes even being visible before HSV PCR shows positive. On the other hand, FLAIR results become more prominent later and are harder to visualize earlier (1). DWI restricted diffusion lesions and FLAIR abnormalities are also useful for differentiation purposes, as the lesions are significantly more frequent in HSE compared to AIE (3).

MRI biomarkers for the detection and differentiation of HSE are a field filled with recent advancements. A 2024 study, Ludovichetti et al. (9), brought forward a new visual biomarker named the "split ADC" sign working upon the DWI/ADC framework, wherein "the cerebral cortex demonstrates restricted diffusion (high DWI signal and low ADC) and the underlying white matter demonstrates facilitated diffusion (high or low DWI signal and high ADC)". The brain locations that the split ADC sign appears in for HSE, as mentioned in the study, are unilateral temporoinsular and bilateral asymmetric temporopolar (9). While MRI may be the gold standard for HSE testing, many improvements can be made to make the process more efficient and accurate. Artificial intelligence (AI) is an influential tool that is capable of being incorporated into our existing MRI technology in order to improve early and differential. diagnoses, too. One particular form of AI is known as deep learning (DL), which is similar to the process. Human characterization and pattern recognition. DL can aid MRI diagnosis because it can efficiently handle large volumes of data of various MRI sequences (10). It is currently possible to attest to a series of marvelous advancements that have been achieved in tapping the power of DL in image analysis, protocol planning, and pathology detection. Here there has also been much advancement lately in using AI-based techniques to help address the main limitation of MRI, which is the relatively long scan time, leading to higher costs as well as motion artifacts (11).

Xiang et al. (10) aimed to design and test a DL algorithm to help them identify cases of AIE from a set of MRI sequences, including T1-weighted imaging, T2-weighted imaging, FLAIR, and DWI. A popular DL model named ResNet-18 was chosen as it was one of the most effective in image classification. Data in the bilateral hippocampal regions was used to train the model and then asked to make an ultimate prediction on the diagnosis between AIE, HSE, and healthy carrier. To evaluate the model's performance and applicability in the clinical setting, three radiologists were brought on to interpret the images from the dataset, too, without knowledge of the patients' clinical information. The study ended up concluding that the trained DL model could diagnose the different conditions with "consistently high performance" and that, at times, may also outperform the radiologists (10). A different study, Zheng et al. (12), set out to use AI in helping to differentiate encephalitis from gliomas. These 2 diseases are not usually difficult to distinguish, but in many documented cases, due to difficulties in reading imaging results, encephalitis has been confused with the diagnosis of a brain tumor, and vice versa, the brain tumor can be confused with encephalitis. Three types of machine learning models were set up, including classical machine learning (CML), DL, and fusion models (containing features of both CML and DL). These models were all trained, developed, and tested on the FLAIR sequence, and then they were compared on their accuracy, sensitivity, and specificity. The study found that the fusion models ended up performing superiorly compared to the other models, with the authors hypothesizing that the combination of CML and DL parameters could enhance the extraction of useful information from these typical MRI images, thus boosting their prediction results (12).

In this qualitative narrative review, we aim to synthesize all current knowledge on the combination of AI with highly developed MRI biomarkers to enhance HSE early and differential diagnosis.

METHODOLOGY

This review was done to look at how AI (artificial intelligence) tools can help in early detection of Herpes simplex encephalitis (HSE). Narrative review was chosen as this topic is still new instead of a systematic review as it includes different areas of medicine, radiology and computer science. The aim is to bring together evidence from different types of studies showing how imaging and AI work together. The search strategy involved a combination of free text terms and Medical Subject Headings (MeSH) obtained from the US National Library of Medicine. Search terms were primarily focused on herpes simplex encephalitis and diagnostic methods, including: “HSV encephalitis”, “herpes simplex encephalitis”, “MRI biomarkers”, “diffusion-weighted imaging (DWI)”, “FLAIR”, “T2-weighted imaging”, and terms relating to artificial intelligence, such as “machine learning”, “deep learning”, “neuroimaging”, and “diagnostic imaging.” Boolean operators (AND/OR) were applied to combine different concepts (e.g “HSV encephalitis AND MRI biomarkers” and “AI AND diagnostic imaging AND encephalitis”) The main databases used for literature search were Google Scholar and PubMed as they cover a large range of articles. The search was focused on papers published from 2015 to 2025 which had both earlier and recent findings and updates (3,4).

INCLUSION CRITERIA

Clinical research studies which have reported MRI biomarkers in patients with HSE including studies that have compared. inter-modal diagnostic accuracy (3,4,9,13). Studies that used an observational method and evaluated the results of neurological imaging, lesion localization, or early. detection by MRI markers (6,7,16). Computational analyses involving the use of AI, machine learning, or deep learning approaches to MRI or. associated neuroimaging data of encephalitis or central nervous system infections (1,11,15). A systematic review or cohort analysis of sufficient size that summarized the findings on MRI or AI in. encephalitis diagnosis (8,14). A combination of such studies provides a possibility to include both clinical and computational evidence. Without which the results will be inefficient.

EXCLUSION CRITERIA

The following were the criteria used to exclude the studies:

-They consisted of animal or non-human subjects.

-They have not included the results in imaging or AI-based HSE diagnosis.

-They concentrated on other etiology-related encephalitis without mentioning HSV or MRI diagnosis.

-They did not provide sufficient patient information, including parsimonious case reports, unless they added pertinent imaging or AI results.

Discussion

It is critical to provide early and accurate diagnosis in the case of herpes simplex virus (HSV) encephalitis as a rapid antiviral therapy can reduce morbidity and mortality (1). MRI imaging is considered as a much better option than other imaging modalities for the early diagnosis of HSE, especially with the advanced versions such as T2 FLAIR and DWI. MRI helps us assess the extent of brain damage, helps us detect abnormalities and rule our differential diagnoses (3). MRI findings are abnormal in most of the HSE cases and are the most sensitive and specific imaging methods (5). Although lab tests and pathological biopsy were a part of standard criteria for diagnosis, it is relatively slower and has chances of false positives. Neuroimaging, therefore, proves to be faster and reliable for differential diagnoses (4). Standard MRI had few limitations which have been addressed by AI techniques like using advanced biomarkers and fusion of deep learning and machine learning, thereby helping us improve diagnosis and distinguish HSE from other neurological disorders (4, 6, 9,15). Another study was a retrospective study of MRI images of people with encephalitis. and temporal lobe abnormalities, indicating that determining whether the abnormalities are confined to one temporal lobe or are bilateral can be useful in identifying the etiology (6). In a different investigation, it was pointed out that HSV-related encephalitis may also include extratemporal areas and showed bihemispheric alterations, instead of confined to the abnormalities of the temporal lobes. Thus, other areas of abnormality could be neglected if only the assessment of the temporal lobes is performed. T2 FLAIR imaging was used as an indication of edema seen in HSV but could also be seen in other brain conditions. In this same study, just using T2-weighted FLAIR is regarded as a limitation and suggested that DWI should be combined for further examination. (6).

MRI images for Herpes encephalitis and autoimmune encephalitis are similar and challenging to diagnosis early stages. Diffusion weighted imaging is an indicator of the molecular movement of water within the tissue. Bani-Sadr et al. (2023) highlighted how DWI helps in distinguishing HSV encephalitis from autoimmune encephalitis since DWI abnormalities are seen in the case of HSE and is rare in the case of autoimmune encephalitis which helps us in differentiating when assessed in early stages of the diseases (3). Cerebral perfusion can also be assessed by non-invasive MRI techniques, which include arterial spin labeling (ASL), which does not require the use of contrast agents, and, therefore, offers a useful source of physiological data. ASL has helped in evaluating brain perfusion and has been applied in differential diagnosis of several diseases (4) MRI helps us assess the extent of brain damage, helps us detect abnormalities and rules our differential diagnosis. MRI findings are abnormal in most of the HSE cases and are the most sensitive and specific imaging technique. Asymmetry hypertense lesions on T2 weighted sequences near to the edema in the mesial temporal, orbitofrontal lobes and the insular cortex can be seen (1). In most cases, the brain MRI reflects areas of T2 and FLAIR hyperintensities afflicting both the cortex and white matter; areas of contrast enhancement may also be detected (5).

Three-dimensional pseudocontinuous arterial spin labeling (3D pCASL) and 3D pCASL are a hybrid of continuous ASL and pulsed ASL that has the benefits of being more efficient in labeling, greater signal-

to-noise ratio, and spatial coverage. HSE patients have shown increased CBF in case of acute and subacute lesions, while decreased CBF in case of chronic lesions on 3D-pCASL. Since HSE has high mortality and morbidity rates, early diagnosis is necessary with the help of neuroimaging examinations like T1W1, T2W1, T2 , FLAIR and DWI. It is advised to perform 3D-pCASL as an initial workup to diagnose and differentiate HSE and start an intervention in highly suspected patients before lab results to expect a better prognosis. 3D-pCASL can be used for differential diagnosis between HSE, MELAS, gliomas and infarct, mostly in acute stages. MELAS and gliomas might mimic the hyper perfusion of HSE on 3D-pCASL, but diagnosis can be made by assessing the location of the lesion, clinical symptoms and history of the patients (4). A novel visual biomarker, split ADC sign which is characterized by restricted diffusion was present on the initial MRI and can mainly be seen in three locations for HSE. The three locations were 3 unilateral temporoinsular, 2 bilateral asymmetric temporopolar and 1 unilateral temporoinsular and insular. In restricted diffusion, ADC (apparent diffusion coefficient) is seen to be low, which means the movement of water molecules is restricted mostly seen in the case of acute HSE. The direct viral invasion of the neuron and cessation of cellular function leads to a restricted diffusion of the cortex which shows up as an ADC split. In the later phases of the infection, congestion gradually decreases which increases perfusion and vasogenic edema, resulting in gradual loss of split ADC sign. As a result, split ADC signs can be used as a potential biomarker in encephalopathy and help differentiate between different types of encephalitis. HSE can be differentiated from AE using ADC since AE shows multifocal ADC throughout brain lobes and in the absence of an isolated temporoinsular which is seen in HSE (9).

Diffusion-weighted imaging (DWI) is very useful in the assessment of cytotoxic and vasogenic edema, and with that it has a high application in the brain lesion assessment and early diagnosis of the lesion (7). DWI, and fluid-attenuated inversion recovery (FLAIR) sequences are mostly found during the acute stage of the infection, and it is easier to see. Temporal or frontal lobes characteristic changes on DWI are highly considered during the diagnosis of HSV encephalitis (1). Among MRI modalities, DWI seems to be the most sensitive sequence to identify HSV encephalitis in the acute phase, and often it reveals hyperintense lesions with limited apparent diffusion coefficient (ADC) values (5). The implementation of artificial intelligence (AI) has additional potential to aid patients that show the symptoms of neurological conditions and help to diagnose a life-threatening condition in a shorter period. Radiomics-based methods are becoming increasingly significant in the neurological domain, and deep learning algorithms are currently being trained to differentiate between imaging data to enhance the differentiation between autoimmune encephalitis (AE) and HSE (15).

Classical machine learning (CML) and deep learning (DL) methods have shown increased levels of sensitivity and specificity in distinguishing HSE amongst other neurological disorders like glioma. These strategies are potentially useful, as they may be used to analyze imaging and clinical data involved in encephalitis and glioma. in study ML models were developed based on FLAIR sequence as its hyperintensities persist for a longer time and reflect cortical hypersignal in case of encephalitis (12). Open-source software like 3D slicers can be used for visualization, segmentation, processing and analysis of 3D images (15). These are combined with deep learning radiomic nomogram (DLRN) and

web calculators can help in better decision making (12). Deep learning Is a subset of AI and has been proven to complement MRI based diagnosis by processing multi sequence data. DL based models could help distinguish HSVE from other conditions like AE as it's always been a challenging task to differentiate them due to similarity in their clinical and radiological characteristics. DWI sequence proved to have a better accuracy compared to other sequences when trained with DL models and is expected to compliment diagnosis on MRI by evaluating a large scale of information. In a retrospective study one of the DL models, ResNet-18 was used for diagnosing encephalitis using 3D MRI sequences, by feeding sequences (T1W1/T2X2/FLAIR/DWI) as independent inputs.

Results showed that these models have shown high accuracy and outperform radiologists' evaluation. Interpreting the DL models have shown that bilateral hippocampal extracted from every sequence could be a potential biomarker to differentiate HSVE from AE. DWI proves to have higher accuracy compared to other sequences due to its hypersensitivity. The fusion model significantly outperformed radiologists' diagnostic performance on average across all matrices in classifying HSVE (10).

According to Sarton et al. (2021) and Defres et al. (2017), MRI abnormalities are also implied to be a predictor of cognitive impairment. Such imaging data can be used with artificial intelligence (AI) models to help clinicians detect patients that are at risk of poor recovery, which would aid in planning long-term management and rehabilitation.

Limitation

There were several barriers observed, like most of these studies are retrospective or single center with modest sample sizes. Image protocols and AI models are not uniform across centers restricting their generalizability (7). Despite the promise of pCASL in diagnosis, its use needs specialized technical assistance in order to be used in large-scale and therapy monitoring which can be challenging in an encephalitis patient. (3).

Pathway of AI integration

Future research should include larger datasets and integrate AI models and prove their accuracy in neuroimaging for quicker and precise diagnosis. The use of advanced biomarkers and multi-sequence MRI are able to complement the old diagnostic techniques; decrease human error and prompt earlier detection of life threatening HSE when combined with AI enhanced models. Development of multimodal AI models should be necessary, which can integrate both imaging and non-imaging data, and help us understand the full spectrum of encephalitis (15,16).

Conclusion

Herpes simplex virus encephalitis (HSE) has been a severe neurological emergency with large morbidity and mortality rates unless treated and detected quickly and accurately. Timely diagnosis is the most important since early antiviral treatment will significantly lower mortality rates of between 70 percent unattended and 10-20 percent treated as well as curb severe neurological sequelae that are experienced by many survivors over time. The state-of-the-art magnetic resonance imaging (MRI) methodologies, particularly diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR), and T2-weighted structural imaging, have proven to be invaluable in early detection of brain abnormalities in HSE, which are usually localized in the medial temporal lobes and limbic system. These imaging biomarkers are crucial in terms of sensitivity and specificity to the extent that computed tomography (CT) can offer and allow clinicians to discriminate between HSE and other conditions that mimic it neurologically, but common characteristics in autoimmune encephalitis and gliomas remain a challenge to diagnosis.

Although MRI is diagnostically valuable, there are certain drawbacks, such as changes in the manifestation of lesions, the necessity to use special sequences, and the complexity of interpretation. The traditional laboratory techniques like cerebrospinal fluid (CSF) polymerase chain reaction (PCR) of HSV DNA is still the gold standard of confirmation but are hampered by false negativity within the early stages of the disease and can be affected by procedural delays. The new molecular methods such as metagenomic next-generation sequencing (mNGS) show potential in quick identification of pathogen in CSF although further validation and resource mobilization is needed to bring them to regular practice.

Artificial intelligence (AI), including deep learning (DL) and classical machine learning (CML), is one of the revolutionary developments in the field of HSE diagnosis. Through the examination of multi-sequence MRI on large scale sample, AI will improve pattern recognition systems, which human beings cannot achieve, resulting in the earlier and more accurate distinction between HSE and other forms of encephalitic or neoplastic pathology. Combining imaging and clinical data in fusion models enhances prediction accuracy and has been demonstrated to be superior to senior radiologists in detecting subtle disease phenotypes including split apparent diffusion coefficient (ADC) sign and bilateral hippocampal abnormalities. Such AI solutions also solve logistic shortcomings of MRI, such as long scan duration, motion artifact, by streamlining imaging protocols and pipelines to automate evaluation. However, there are still several challenges on the path to the full adoption of AI in clinical processes. Most of the research up to now is retrospective, single center, with small sample sizes, which causes heterogeneous imaging protocols and AI models that cannot be generalized. To confirm AI diagnostic accuracy, reproducibility and clinical utility, standardization, bigger multicenter datasets, and prospective trials are both required. Also, by creating multimodal AI models which combine imaging biomarkers with non-imaging clinical information e.g. CSF findings, serological markers, and patient demographics, one can provide a better picture of encephalitis pathophysiology and improve personalized patient care.

To conclude, the combination of the use of sophisticated MRI biomarkers and the latest AI technology promises ushering in a new age in the early and differentiation diagnosis of HSE. It is expected that this integration will decrease the time taken to make the diagnosis, increase the ability to distinguish it in the setting with similar conditions, and eventually improve clinical outcomes due to the provision of antiviral treatment and individualized long-term care plans. Further investigation and technological advancement are urgent in order to address the existing shortcomings and achieve maximum clinical potential of these innovations in fighting this devastating central nervous system infection.

Acknowledge

The authors confirm that all individuals listed as authors made substantial, equal contributions to the development of this work, including the abstract, introduction, methodology, discussion, and conclusion. The collaborative nature of this project reflects the shared responsibility and joint effort of all team members.

References:

1. Bradshaw MJ, Venkatesan A. Herpes Simplex Virus-1 Encephalitis in Adults: Pathophysiology, Diagnosis, and Management. Neurotherapeutics. 2016 Jun 1;13(3):493–508.

2. Tyler KL. Acute Viral Encephalitis. N Engl J Med. 2018 Aug 9;379(6):557–66.

3.Bani-Sadr A, Ruin-Allinieu MC, Brisset JC, Ducray F, Joubert B, Picard G, et al. Contribution of diffusion-weighted imaging to distinguish herpetic encephalitis from autoimmune encephalitis at an early stage. J Neuroradiol. 2023 May 1;50(3):288–92.

4. Li R, Shi PA, Liu TF, Li Y, Wang Y, Wu K, et al. Role of 3D Pseudocontinuous Arterial Spin Labeling Perfusion in the Diagnosis and Follow-Up in Patients with Herpes Simplex Encephalitis. AJNR Am J Neuroradiol. 2019 Nov;40(11):1901–7.

5.Bertrand A, Leclercq D, Martinez-Almoyna L, Girard N, Stahl JP, De-Broucker T. MR imaging of adult acute infectious encephalitis. Médecine Mal Infect. 2017 May 1;47(3):195–205.

6. Defres S, Keller SS, Das K, Vidyasagar R, Parkes LM, Burnside G, et al. A Feasibility Study of Quantifying Longitudinal Brain Changes in Herpes Simplex Virus (HSV) Encephalitis Using Magnetic Resonance Imaging (MRI) and Stereology. PLOS ONE. 2017 Jan 26;12(1):e0170215.

7.Sarton B, Jaquet P, Belkacemi D, de Montmollin E, Bonneville F, Sazio C, et al. Assessment of Magnetic Resonance Imaging Changes and Functional Outcomes Among Adults With Severe Herpes Simplex Encephalitis. JAMA Netw Open. 2021 Jul 27;4(7):e2114328.

8.Tan Y, Liu M, He L. Clinical and MRI differential analysis of autoimmune encephalitis and viral encephalitis. J Taibah Univ Med Sci. 2022 Oct 11;18(2):271–8.

9.Ludoviche R, Nierobisch N, Achangwa NR, De Vere-Tyndall A, Fierstra J, Reimann R, et al. The split apparent diffusion coefficient sign: A novel magnetic resonance imaging biomarker for cortical pathology with possible implications in autoimmune encephalitis. Neuroradiol J. 2024 Apr;37(2):206–13.

10.Xiang Y, Zeng C, Liu B, Tan W, Wu J, Hu X, et al. Deep Learning-Enabled Identification of Autoimmune Encephalitis on 3D Multi-Sequence MRI. J Magn Reson Imaging. 2022 Apr;55(4):1082–92.

11.Shimron E, Perlman O. AI in MRI: Computational Frameworks for a Faster, Optimized, and Automated Imaging Workflow. Bioengineering. 2023 Apr 20;10(4):492.

12. Zheng F, Yin P, Yang L, Wang Y, Hao W, Hao Q, et al. MRI-Based Machine Learning Fusion Models to Distinguish Encephalitis and Gliomas. J Imaging Inform Med. 2024 Jan 12;37(2):653–65.

13. Hermetter C, Fazekas F, Hochmeister S. Systematic review: syndromes, early diagnosis, and treatment in autoimmune encephalitis. Front Neurol. 2018 Sep 4;9:706. doi:10.3389/fneur.2018.00706.

14. Bokhari SFH, Almadhoun MIKH, Khan MU, Ahmad S, Awan M, Imran MM, Bashir M, Tariq MR, Imran M, Khalid MO. Emerging biomarkers for the early detection of autoimmune encephalitis: a narrative review. Cureus. 2024 Sep 9;16(9):e69038. doi:10.7759/cureus.69038.

15. Musigmann M, Spiekers C, Stake J, Akkurt BH, Mora NGN, Sartoretti T, Heindel W, Mannil M. Detection of antibodies in suspected autoimmune encephalitis diseases using machine learning. Sci Rep. 2025 Mar 31;15:10998. doi:10.1038/s41598-025-95815-z.

16.Mulate ST, Tasamma AT, Fole EB, Anbessie ZM, Mengesha MA, Muleta RT. Herpes Simplex Encephalitis Complicated With Vasculitis in a Young Male: A Case Report. Clin Case Rep. 2024 Nov 29;12(12):e9603. doi:10.1002/ccr3.9603.