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# Neuroimaging for Stroke Patients: How it Affects the Recovery Process

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## Abstract

**Background:** Kratom (Mitragyna speciosa), a psychoactive plant with both opioid and stimulant properties, has gained popularity in the U.S. for self-treatment of a wide range of conditions, including pain, opioid dependency, withdrawal, and mood disorders. Despite its increasing use, kratom toxicity remains poorly understood by many healthcare providers, complicating emergency care. While evidence does exist supporting the benefits of kratom for conditions such as pain and withdrawal, it remains an under-studied substance with a potential for abuse.

**Objective:** This review aims to summarize the current literature on kratom's pharmacology, clinical presentation, diagnostic considerations, and management in the ED.

**Methods:** A systematic review of case reports, observational studies, and toxicology literature will be conducted using PubMed, Embase, and Google Scholar. Relevant studies on kratom-related ED visits, adverse effects, withdrawal syndromes, and treatment strategies will be analyzed.

**Discussion:** Kratom toxicity presents variably, ranging from mild symptoms (tachycardia, hypertension, agitation) to severe effects (seizures, respiratory depression, hepatotoxicity). Diagnostic challenges arise due to the absence of standardized testing. Management is primarily supportive, but opioid withdrawal treatment and benzodiazepines for agitation or seizures may be necessary. The potential for drug interactions and adulterants further complicates care.

**Conclusion:** Kratom use poses an emerging challenge in emergency medicine, necessitating greater awareness and standardized treatment protocols. This review aims to provide ED providers with an evidence-based understanding of kratom use, its clinical effects, diagnostic challenges, and best practices for management in acute care settings.

**Key Words:** opioid and stimulant properties; opioid dependency; mood disorders; kratom's pharmacology; tachycardia; hypertension; agitation

## Introduction

Stroke is one of the leading causes of death and disability worldwide, imposing a large economic and emotional burden on patients and their families. Stroke patients often face various sequelae, including motor dysfunction, cognitive impairment, and emotional disorders, which seriously impacts their quality of life. One of the severe consequences of acute ischemic stroke (AIS) is cerebral edema, characterized by the abnormal increase in water content within the brain interstitial space [2, 3]. Cerebral edema plays a pivotal role in the progression of ischemic brain infarction and is associated with adverse clinical outcomes, including neurological deterioration and poor functional recovery [4].

In recent years, researchers have focused on exploring novel neuroimaging methods capable of quantitatively assessing early brain edema after AIS. Another complication, aphasia, arises from the inability to understand and regulate language after injury to certain areas of the brain [5]. Approximately 35-40% of adults admitted to a hospital because of strokes are diagnosed with aphasia [6].

Recently, newly developed techniques, such as diffusion tensor imaging (DTI), voxel-based lesion symptom mapping, and functional magnetic resonance imaging (fMRI) have been used to study the effects of brain lesion location and sizes on aphasia [7]. This article will examine how neuroimaging in stroke patients informs and affects the recovery process.

### Pathophysiology of Stroke and Recovery Challenges

Acute Ischemic Stroke (AIS) is the loss of function caused by an inadequate supply of blood to cerebral tissue. This inadequate blood supply is the result of a blockage from clots caused by atrial fibrillation or from thrombi that develop on fatty deposits known as atherosclerotic plaque [8]. Ischemia causes dysregulation of sodium transport channels, leading to a disruption of normal biochemical gradients. Intracellular sodium concentration rises, causing osmotic forces to pull water into the cell via aquaporin channels, leading to cellular lysis and cell death [9]. This swelling of brain tissue — cerebral edema— leads to increased intracranial pressure (ICP) and can result in herniation. Brain tissue shifting can lead to secondary infarctions and intracranial hemorrhage through the stretching and tearing of cerebral vessels [10]. The severity of cerebral edema has also been shown to strongly correlate with poor clinical outcomes. Han et al. demonstrated that net water uptake (NWU) within the ischemic core reflects the severity of ionic and vasogenic edema, which in turn is related to early damage to the blood-brain barrier, ion channel disturbances, and other complex mechanisms— all of which may contribute to poor outcome of patients [11]. As cerebral edema can evolve rapidly in the first 24-72 hours post-stroke, early detection is critical in guiding treatment decisions and improving functional outcomes.

## Common Functional Impairments Post-Stroke

Due to cerebral damage and edema, stroke survivors frequently experience motor impairments that impact long-term recovery. These deficits often manifest as weakness, spasticity, or loss of fine motor control, which can limit functional independence. Upper extremity impairment is common, affecting 50-80% in the acute phase after stroke. Rafsten et al. found that dysfunction of limb movement in the impaired arm was significantly associated with impaired postural balance [12]. Cognitive deficits are also common post-stroke. The AHA/ASA note that "post-stroke cognitive impairment is common in the first year after stroke, occurring in up to 60% of stroke survivors" [13]. These impairments, affecting patient memory, attention, and executive function, significantly contribute to long-term disability and loss of independence. Language dysfunction, particularly aphasia, is another prominent sequela of stroke. Aphasia affects a range of language functions including fluency, comprehension, naming and repetition, although the type and severity are dependent on lesion location. For example, Kang et al. found that subcortical lesions tend to result in milder aphasia, whereas cortical lesions involving Broca's or Wernicke's areas, as well as the insular cortex, are associated with more severe language impairments [14].

## Role of Neuroimaging in Stroke Management

*Traditional Imaging Modalities*

Neuroimaging plays a crucial role in guiding clinical decisions with traditional modalities, such as CT and MRI, being at the forefront. In the initial stages, non-contrast computed tomography (NCCT) is employed primarily to exclude hemorrhagic stroke, a critical step before administering thrombolytics [15]. In the early few hours after AIS however, the brain parenchyma is often normal on CT. Computed tomography angiography (CTA) and computed tomography perfusion (CTP) have become essential in overcoming this limitation. The identification of intracranial arterial occlusions - particularly large vessel occlusions (LVOs) - on CTA are indicative of acute ischemic stroke and inform the use of endovascular thrombectomy. CTP, on the other hand, provides functional maps containing parameters such as cerebral blood flow and cerebral blood volume to identify the ischemic core and salvageable penumbra (16). Although CT and its advanced modalities remain the standard in the hyperacute phase of AIS due to speed and availability, magnetic resonance imaging (MRI) provides greater sensitivity in detecting early ischemic changes. Through the use of Diffusion-Weighted Imaging (DWI, an estimate of infarct volume can be made, allowing early diagnosis. Additionally, Perfusion-Weighted Imaging (PWI) can detect cerebral blood flow abnormalities, and when combined with DWI, can help differentiate the ischemic core from the penumbra. Magnetic Resonance Angiography (MRA) is also used to complement these findings by identifying arterial occlusions [17].

This multimodal MRI approach - DWI, PWI, and MRA - provides comprehensive assessment that rivals CT-based protocols, with the added benefit of avoiding ionizing radiation and contrast exposure. Despite these advantages, MRI use remains limited due to accessibility issues, longer setup times, and contraindications such as implanted devices. Nonetheless, MRI's ability to detect early ischemic injury and greater diagnostic precision make it an invaluable modality in stroke imaging.

***Advanced Neuroimaging Techniques* -** DTI, fMRI, VLSM + assessment (lesion mapping, plasticity, etc.)

While CT and MRI remain central in acute stroke management, advanced neuroimaging techniques - such as diffusion tensor imaging (DTI), functional MRI (fMRI), and voxel-based lesion-symptom mapping (VLSM) offer a more detailed understanding of brain injury and recovery trajectories. Diffusion tensor imaging characterizes microstructural integrity by assessing the directional movement of water along white matter tracts. The fractional anisotropy (FA) value, a DTI-derived metric, reflects this directionality; higher FA values indicate well-organized white matter, while reduced values indicate axonal disruption or demyelination [18]. DTI is particularly valuable for predicting motor outcomes, as decreased FA in the corticospinal tract (CST) - a key pathway frequently affected by stroke - has been consistently associated with poorer motor recovery [19].

Functional MRI (fMRI) offers a noninvasive method to measure neural activity and functional connectivity through blood oxygen level-dependent (BOLD) signals, offering insight into how the brain reorganizes after a stroke. Li et al. demonstrated a causal relationship between resting-state functional connectivity, particularly in language-related (inferior frontal gyrus, posterior middle temporal gyrus) and motor-related (supplementary motor area) brain regions, and poor functional recovery following ischemic stroke [20[. This only further highlights the potential role of fMRI for predicting and targeting aphasia and motor deficits. Similarly, Falconer et al. examined how functional connectivity within broader brain networks can predict responsiveness to therapy. Higher functional connectivity in the dorsal attention network- involved in voluntarily directing attention towards relevant stimuli - and salience network- involved in detecting and filtering sensory information - enhanced the effectiveness of language therapy in chronic aphasia patients [21]. These findings highlight the potential of fMRI-based biomarkers to forecast individual recovery and guide targeted therapies. Resting state fMRI has also been used to characterize post-stroke plasticity.

Building on this, Wu et al. applied a multilayer dynamic network analysis to rs-fMRI data from stroke patients with varying levels of clinical severity. They found that mild stroke patients showed reduced recruitment in the visual and limbic networks; whereas, severe cases demonstrated reduced recruitment in the sensorimotor and limbic networks. This suggests that stroke severity is associated with different patterns of time-varying functional network reorganization, where segregation increases between some systems and integration increases or decreases between others [22]. FMRI's unique ability to capture dynamic brain reorganization may eventually serve as a clinical tool for monitoring recovery progress and tailoring interventions to patients' neural profiles.

Voxel-based lesion -symptom mapping (VLSM) is another method used to link specific brain lesion locations to functional deficits at a voxel-wise level. Na et al. conducted a coordinate-based meta-analysis of over 2000 patients with post-stroke aphasia, identifying distinct lesion patterns associated with specific language tasks. Their findings suggest that lesions in the dorsal pathway (e.g., inferior frontal gyrus, precentral gyrus, and supramarginal gyrus) impair speech production and phonological processing; whereas, ventral pathway lesions (e.g., anterior temporal lobe, middle temporal gyrus) were linked to deficits in comprehension. The study further employed a meta-analytic coactivation framework to relate lesion sites to functional networks in healthy individuals - integrating lesion- deficit mapping with insights from functional neuroimaging. VLSM further revealed task-specific lesion profiles linking language deficits to dorsal lesions and further identifying the posterior superior temporal gyrus's involvement in repetition deficits- a hallmark of conduction aphasia [23]. The use of lesion mapping with functional models of language suggests that VLSM can inform prognosis and rehabilitation targets while clarifying brain-behavior relationships.

### Clinical Implications of Imaging Findings

*Imaging Biomarkers and Recovery Prediction*

Advanced neuroimaging techniques are increasingly being applied in clinical settings to guide prognosis and optimize rehabilitation strategies following stroke. Building upon diffusion tensor imaging, DTI tractography is commonly used to reconstruct three-dimensional images of white matter tracts—such as the corticospinal tract and arcuate fasciculus—allowing clinicians to evaluate the structural integrity of motor and language-related networks [19, 24]. Disruption or degeneration of these pathways can provide insight into a patient's possible complications, recovery trajectory, and the potential for functional recovery. For example, a partially intact CST might suggest the potential for recovery through aggressive therapy, whereas complete disconnection may shift the therapeutic focus towards compensatory strategies.

A multimodal approach combining fMRI and VLSM with DTI tractography can refine patient-specific rehabilitation protocols and allow for a more holistic understanding of post-stroke recovery. While VLSM identifies key brain regions responsible for specific functions and fMRI tracks functional network reorganization, tractography depicts the underlying white matter pathways that connect these regions [22, 23]. Currently, these neuroimaging biomarkers assist clinicians in tailoring rehabilitation programs, improving prognostic accuracy, and optimizing treatment intensity based on individual brain structure and function.

### Guided Rehabilitation Strategies

Specific rehabilitation modalities are optimally matched to neuroimaging biomarkers for a precision-guided approach that enhances functional outcomes. One of the most commonly utilized treatments is constraint-induced movement therapy (CIMT), during which the unaffected extremities are immobilized and the affected extremities perform daily living activities. In a study conducted by Marumoto et al., diffusion tensor imaging was used to predict the outcome of CIMT for stroke patients. Higher fractional anisotropy (FA) ratios in the posterior limb of the internal capsule- a core portion of the CST- were strongly correlated with better outcomes after CIMT [25]. This highlights the potential for DTI to guide patient selection for CIMT and other therapies.

Another promising example of image-guided therapy is transcranial direct current stimulation (tDCS), a non-invasive neuromodulation technique that can be used to augment post-stroke aphasia recovery. In a pilot study by Soliman et al., bi-hemispheric tDCS was administered to patients with subacute post-stroke aphasia, targeting the left affected Broca's area with anodal stimulation and the contralesional right Broca's homologue with cathodal stimulation. The study used DTI-based tractography to show that significant FA changes in the right hemisphere after treatment were strongly correlated with improvements in language fluency [26]. Advanced diffusion imaging, when coupled with tDCS protocols, has the potential to guide individualized aphasia rehabilitation strategies and monitor structural changes that correlate with functional improvements.

## Limitations to Clinical Use

Despite the growing utility of advanced neuroimaging techniques in stroke recovery, several limitations hinder their widespread clinical application. Accessibility to techniques such as diffusion tensor imaging, functional MRI, and voxel-based lesion-symptom mapping is confined to large academic medical centers and is limited in rural and community settings.

Time constraints during acute stroke also limit the use of advanced imaging techniques because of their large acquisition and processing requirements. In hyperacute settings, imaging with CT remains the standard due to its speed and availability allowing clinicians to make urgent treatment decisions such as thrombolysis or thrombectomy. The high cost of MRI- based modalities and the need for trained personnel further limits their feasibility in routine care, especially in areas where healthcare resources are limited.

Lastly, although numerous studies have demonstrated strong correlations between neuroimaging biomarkers and clinical outcomes, evidence that these imaging techniques directly improve recovery through tailored interventions remains limited. The lack of large-scale randomized controlled trials integrating advanced neuroimaging into treatment decision-making continues to limit their inclusion in standard stroke care protocols.

## Conclusion

Ultimately, the clinical application of these advanced neuroimaging methods allows for a precision medicine approach to stroke care. These techniques enable tailored, network-specific interventions that align with each patient's unique pattern of brain injury and plasticity potential. Future studies should focus on validating outcome-based biomarkers through large-scale clinical trials, and developing pragmatic frameworks that integrate neuroimaging into routine stroke rehabilitation planning.

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