Review

Clinical Recognition And Management Of Emergencies In Movement Disorders

Jamir Pitton Rissardo *, Ibrahim Khalil, Ahmed Farid Gadelmawla, Ola Dafaalla Mohamed, Mohamed Yousif Elamin, Reem Sayad, Ana Letícia Fornari Caprara

Posted Date: 24 January 2025

doi: 10.20944/preprints202501.1811.v1

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 doi:10.20944/preprints202501.1811.v1

Review

Clinical Recognition and Management of Emergencies in Movement Disorders

Jamir Pitton Rissardo [1,*], Ibrahim Khalil [2], Ahmed Farid Gadelmawla [3], Ola Dafaalla Mohamed [4], Mohamed Yousif Elamin [4], Reem Sayad [5] and Ana Letícia Fornari Caprara [1]

[1] Neurology Department, Cooper University Hospital, NJ 08103, USA
[2] Faculty of Medicine, Alexandria University, Alexandria 5372066, Egypt
[3] Faculty of Medicine, Menoufia University, Menoufia 6132720, Egypt
[4] Faculty of Medicine, University of Khartoum, Al-Qasr Avenue Street 11111, Khartoum, Sudan
[5] Faculty of Medicine, Assiut University, Assiut 71515, Egypt
* Correspondence: jamirrissardo@gmail.com

Abstract: Movement disorders, such as Parkinson's disease (PD), dystonia, and Huntington's disease, can occasionally lead to medical emergencies that require recognition and treatment. These emergencies may arise from the natural progression of the disease or complications associated with treatment. In PD, for example, a sudden worsening of motor symptoms—often referred to as "off" periods—can result in severe immobility, leading to falls or even aspiration pneumonia. Additionally, conditions like neuroleptic malignant syndrome, a rare but life-threatening reaction to dopaminergic medications, can manifest with fever, muscle rigidity, and altered mental status, making it crucial for timely diagnosis and intervention. Another emergency in movement disorders is status dystonicus, a severe and sustained dystonic episode that can occur in individuals with dystonia. This condition can lead to muscle breakdown, respiratory compromise, and even rhabdomyolysis, necessitating intensive care. Sudden exacerbations of chorea, such as in Huntington's disease, can also precipitate emergencies, especially if the movements are so severe that they cause self-injury and significantly impact the quality of life of patients. These emergencies underscore the importance of having an acute management plan for patients with known movement disorders. Timely intervention in these situations is critical to prevent further complications. Noteworthy, the emergency department physician should first assess life-threatening conditions and be able to provide a detailed phenomenological description of the abnormal movement observed.

Keywords: movement disorder; emergency; urgency; status dystonicus; neuroleptic malignant syndrome; serotoninergic syndrome; dyskinesias

1. Introduction

Emergencies in movement disorders are a subject scarcely discussed in the literature. Movement disorders emergencies generally comprise an acute or subacute worsening of a motor symptom and the subject has received more attention in the last decade. In clinical practice, the neurohospitalist receives commonly urgent consults regarding myoclonus, choreiform movements, and dystonia, as well as less urgent consults for cases of tremor and parkinsonism [1]. In the current review, we will narratively assess the published literature about hyperkinetic and hypokinetic movement disorder emergencies.

2. Clinical Presentation and Diagnosis

2.1. Neuroleptic Malignant Syndrome

 doi:10.20944/preprints202501.1811.v1

Generally, neuroleptic malignant syndrome (NMS) is observed within 28 days of taking antipsychotics and includes altered mental status as a clinical tetrad with hyperthermia, rigidity, and dysautonomia. In the early stages, changes in mental state and rigidity of muscles occur, later accompanied by fevers and dysautonomia, which begins with tachycardia followed by labile blood pressure [2]. The primary diagnostic criteria for diagnosing NMS according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, criteria include exposition to dopamine-blocking agents, severe muscle rigidity, and fever. The other symptoms that are included in the diagnosis are diaphoresis, dysphagia, tremor, incontinence, altered level of consciousness, mutism, tachycardia, elevated or labile blood pressure, leukocytosis, and elevated creatine phosphokinase. Although renal dysfunction usually progresses rapidly and CK is elevated, when a clinical diagnosis is made, laboratory data usually supports a diagnosis of rhabdomyolysis. The extent of the disease usually correlates directly with the degree of CK elevation and may be profound. Leukocytosis is often present and consists of white blood cell counts with a left shift in the range of 10,000 to 40,000/mm3. Transaminases may be slightly elevated as well. Neuroimaging and even lumbar puncture may also be required for patients whose diagnosis is less precise to rule out structural and infectious diagnoses. Although most cases are diagnosed clinically, further laboratory testing, such as a lithium level and a drug abuse screening, may also be helpful in certain circumstances [3]. The most important differential diagnoses are serotonergic syndrome, malignant hyperthermia, and catatonia [4].

2.2. Parkinsonism-Hyperpyrexia Syndrome

Symptoms can appear anywhere from 18 hours up to 7 days from the change in dopaminergic medication. Patients with parkinsonism-hyperpyrexia syndrome (PHS) may have a slightly more delayed onset than patients with NMS [5]. Clinical features of PHS are similar to those of NMS, though there may be a few more parkinsonian features early in its course. Rigidity, stupor, and hyperthermia of an elderly PD patient in a state of levodopa withdrawal are a classic presentation of PHS [6]. Rigidity, tremors, akinesia, hyperthermia, agitation, delirium, stupor, and coma usually occur in a sequence. Tachycardia is one of the early signs of dysautonomia. Other symptoms include blood pressure fluctuation, tachypnea, and sweating. Hyperthermia results from a combination of central thermoregulatory dysfunction and muscular hyperactivity. Myoclonus and seizures are not uncommon. CK and white cell counts are usually raised [6]. Diagnosis is mainly by exclusion, and the clinical diagnostic criteria used for NMS can be used here with the caveats listed above. The general practitioner should be aware of the social circumstances since older PD patients with cognitive impairment may omit doses and develop PHS. The most consistent features appear to be rigidity, hyperpyrexia, and altered consciousness [7]. No laboratory findings have been consistently detected, but elevations in CK and leukocytosis are less prominent than in NMS. Elevated liver transamination and metabolic acidosis may be present. Coagulopathies, infections, and other toxic metabolic syndromes must be assessed to rule out other causes and manage complications [8].

2.3. Serotonin Syndrome

The most commonly noted clinical features of serotonin syndrome (SS) include change in mental status, agitation, myoclonus, hyperreflexia, diaphoresis, shivering, tremors, diarrhea, incoordination, and fever. These represent a spectrum with mild serotonin toxicity on one end and a fulminant SS on the other. Neuromuscular irritability manifesting as clonus in some form is the most important diagnostic feature of SS [9]. Autonomic dysfunction features are expected in NMS and MC but are often mild. Spontaneous myoclonus may involve the limbs, face, head, and neck; less commonly, the whole body is affected in severe disorder cases. Severe spontaneous myoclonus can appear “rhythmic” and resemble tremors. Opsoclonus, or ocular clonus, is the involuntary large amplitude and nonrhythmic jerking of eye movements in multidirectional. It represents a cause of considerable distress for patients due to oscillopsia, the subjective jumping up and down sense of objects in the visual field [10]. Myoclonus is invariably associated with exaggerated deep tendon reflexes.

 doi:10.20944/preprints202501.1811.v1

Anticholinergic toxicity is a close differential diagnosis that presents similarly with pupillary dilation, delirium, dry mucosa, and skin erythema. However, sweating, hyperactive bowels, diarrhea, hyperreflexia, and clonus distinguish SS from anticholinergic syndrome, NMS, and MC [10]. Clinical diagnosis of serotonin syndrome is generally made according to the history of the use of serotonergic drugs or illicit substances by the patient, dose change, or addition of new medications, supplemented by physical examination [11]. There are no specific biomarker for serotonin syndrome, although nonspecific laboratory abnormalities have been described, including leukocytosis, low bicarbonate, elevated creatinine, and elevated transaminases [12]. Several diagnostic criteria have been suggested for classifying serotonin syndrome. The Hunter Serotonin Toxicity Criteria, which replaced the earlier Sternbach Criteria, are the most sensitive and specific. It is sensitive to 84% and specific to 97% compared to the diagnostic gold standard of serotonin syndrome, which is a diagnosis made by a medical toxicologist [13]. This makes it challenging to distinguish mild serotonin syndrome from a host of other medical conditions and side effects; hence, the Hunter Criteria cannot be applied here [11].

2.4. Malignant Catatonia

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, symptoms of catatonia include stupor—no psychomotor activity, not relating actively to the environment; catalepsy-passive induction of a posture held against gravity; waxy flexibility—slight, even resistance to positioning by the examiner; mutism—no verbal response or very little, excluded if known aphasia; negativism—opposition or no response to instructions or external stimuli; mannerism—spontaneous and active maintenance of a posture against gravity; stereotypy: repetitive, abnormally frequent, non-goal-directed movements; agitation, grimacing; echolalia: mimicking another's speech; and echopraxia: mimicking another's movements [14]. The diagnosis is based on three or more of these symptoms; malignant catatonia includes these symptoms with fever and dysautonomia symptoms such as hyperthermia, tachycardia, and blood pressure fluctuations [15].

2.5. Status Dystonicus

Status dystonicus is the development of increasingly frequent or continuous severe episodes of generalized dystonic spasms (contractions) that require immediate attention, often in a hospital. Recent phenomenological classification categorizes episodes of status dystonicus into tonic-primarily sustained contractions and abnormal postures or phasic-rapid and repetitive dystonic contraction phenotypes. The tonic phenotype predominates in males and secondary (acquired) dystonias, with possibly a poorer prognosis [16]. Status dystonicus movements may overlap with other, more prominent hyperkinesias, such as choreoathetosis, complicating objective recognition [17].

To date, there has been no internationally accepted definition of status dystonicus. Manji et al. suggested the following criteria, which include life-threatening complications and bulbar weakness causing a threat to airway patency [18]. Progressive impairment of respiratory function leading to respiratory failure. Metabolic abnormalities. Exhaustion and pain.

2.6. Myoclonus

Myoclonus is clinically defined as sudden, brief, shock-like involuntary movements resulting from muscular contractions or inhibitions [19]. Electromyography shows myoclonus as a brief discharge that is usually so synchronous that it looks very different from a voluntary ballistic electromyography (EMG) discharge. It has a distinctive monophasic feature, with only one component of the movement active and the remainder passively returning to baseline [20]. The clinical presentation differs based on the kind of myoclonus. (1) Physiologic myoclonus includes a normal phenomenon—there is minimal or no associated disability, and the physical exam shows no relevant abnormality [20]. (2) Essential myoclonus refers to myoclonus as the major or sole clinical finding; dystonia may form an important component of this variety [20]. (3) Epileptic myoclonus

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refers to the appearance of myoclonus in the context of a chronic seizure disorder—epilepsy. Myoclonus alone may constitute an entire seizure, the sole manifestation of a seizure, or part of a complex epileptic syndrome in its entirety. (4) Symptomatic, that is to say, secondary myoclonus, a diagnosable neurologic or non-neurologic disorder usually exists. Some clinical associations that commonly occur with symptomatic myoclonus include cognitive changes and ataxia [21]. Clinical characteristics of myoclonus can be described clinically—that is, distribution, temporal, and activation profiles—by a thorough history including medications taken, toxin exposure, recent infections, and known predispositions, along with careful physical examination. This is followed by basic, widely available examinations such as blood, urine, antibody tests, and brain magnetic resonance imaging to decrease the differential diagnoses [22]. According to the clinical scenario, further neurophysiologic testing may include surface EMG or electroencephalography (EEG)-EMG polygraphy and advanced and emerging testing [22].

2.7. Tics

A tic is a sudden, repetitive, non-rhythmic, stereotyped motor movement or vocalization involving specific muscle groups. Tics can be identified based on anatomical location, number, frequency, and duration. Another valid descriptor is the intensity or "forcefulness" of the tic, as some tics call attention to themselves simply by their exaggerated and forceful quality. Tics typically begin during the first decade of life between 4-6 years with simple motor movements such as eye blinking, nose twitching, or facial grimaces. Motor tics tend to spread rostrally over time. Similarly, vocal tics begin with simple throat clearing, sniffing, or word fragments [23].

2.8. Chorea and Ballism

Chorea is a hyperkinetic movement disorder characterized by rapid and unpredictable contractions, primarily within the distal limbs but also involving the face and trunk. Accordingly, movements are involuntary and non-patterned in structure, with various speeds, timing, and directions flowing from one body part to another and, in minor cases, the appearance of fidgeting. Chorea can be differentiated from tremor and dystonia by its randomness and flow [24].

2.9. Drug-Induced Movement Disorder

The usual presentation in the emergency department (ED) with a movement disorder in a previously healthy individual should raise attention to drug-induced movement disorders. The patient should be asked about recent medication started or changes in doses, and this should include drugs of abuse. Common presentations include tremors and chorea related to steroids [25], cocaine-induced dystonia [26], gabapentin-induced myoclonus [27], phenytoin-induced dyskinesias [28], and valproate-induced tremors [29]. If there is no specific literature about the medication, the medication should be discontinued. Also, it is worth remembering the class effects of different medications.

3. Management Strategies

3.1. Neuroleptic Malignant Syndrome

The most crucial step is discontinuing the offending agent, followed by initiating supportive therapy. This includes rigorous cooling and correcting volume deficits and electrolyte imbalances. Patients are more likely to develop cardiac dysrhythmias and respiratory failure as a result of chest wall rigidity [3]. More severe instances are treated with empiric pharmacological therapy. Meta-analyses and case reports may shorten the course and minimize morbidity and mortality. Bromocriptine, a dopamine agonist, is administered orally or through a gastric tube to reverse the hypodopaminergic condition. Dantrolene, a muscle relaxant, can be taken intravenously or orally in less severe situations [3]. Benzodiazepines can also be used to control agitation. If the syndrome is caused by a quick withdrawal of dopaminergic drugs, resuming the medication may alleviate

 doi:10.20944/preprints202501.1811.v1

symptoms. Electroconvulsive therapy has also been reported to be beneficial in refractory patients. Patients should be admitted to an intensive care unit and closely monitored [30]. For a complete description of the management strategies for movement disorders emergencies, consider reading Table 1.

Table 1. Management Strategies for Movement Disorder Emergencies.

Condition	Immediate Interventions	Pharmacological Treatment	Non-Pharmacological Treatment
Neuroleptic malignant syndrome	Discontinue offending medication; ensure ABCs; monitor vital signs.	Dantrolene (for muscle rigidity), supportive care (e.g., hydration, cooling measures).	Discontinue offending medication, avoid future use of neuroleptics.
Parkinsonism-hyperpyrexia syndrome	Discontinue offending medication; ensure ABCs; monitor vital signs.	Supportive care (e.g., hydration, cooling measures), dopamine agonists (if appropriate).	Avoid future use of offending medication.
Serotonin syndrome	Discontinue offending medication; ensure ABCs; monitor vital signs.	Cyproheptadine (for serotonin receptor antagonism), supportive care (e.g., hydration, cooling measures).	Discontinue offending medication, avoid future use of serotonergic drugs.
Malignant catatonia	Ensure ABCs; monitor vital signs; consider benzodiazepines or ECT.	Benzodiazepines (e.g., lorazepam, diazepam), ECT (if severe or unresponsive to medications).	Supportive care, avoid precipitating factors.
Status dystonicus	Ensure ABCs; monitor vital signs; administer anticholinergics or benzodiazepines.	Anticholinergics (e.g., benztropine, trihexyphenidyl), benzodiazepines (e.g., lorazepam, diazepam).	Supportive care, avoid precipitating factors.
Myoclonus	Ensure ABCs; monitor vital signs; consider anticonvulsants or neuroleptics.	Anticonvulsants (e.g., valproic acid, clonazepam), neuroleptics (e.g., risperidone, haloperidol).	Supportive care, avoid precipitating factors.
Tics	Ensure ABCs; monitor vital signs; consider temporary use of alpha-blockers or antipsychotics.	Alpha-blockers (e.g., clonidine, guanfacine), antipsychotics (e.g., risperidone, haloperidol).	Behavioral therapy, deep brain stimulation.
Chorea and ballism	Ensure ABCs; monitor vital signs; adjust medication dosage.	Antipsychotics (e.g., risperidone, haloperidol).	Supportive care, avoid precipitating factors.

3.2. Parkinsonism-Hyperpyrexia Syndrome

 doi:10.20944/preprints202501.1811.v1

Patients with PHS require close monitoring in the critical care unit. Intravenous fluids, electrolyte replacement, antipyretics, cooling treatments, judicious use of benzodiazepines, and gradual return of the previous anti-parkinsonian drug regimen are all part of ICU management [31]. A nasogastric tube can assist individuals with dysphagia in receiving dopaminergic treatment. If this fails, alternative therapies include intramuscular or intravenous apomorphine and transdermal rotigotine. It is critical to monitor vital signs and serum muscle enzymes, renal function, and coagulation function regularly [31].

3.3. Serotonin Syndrome

The primary method of treatment for serotonin syndromes is stopping all serotonergic medications right away and giving supportive care to keep vital signs stable. When adequately treated, serotonin syndrome typically disappears in less than 24 hours without any aftereffects [11]. In moderate situations, benzodiazepines for sedation, if necessary, observation, supportive care, and stopping serotonergic medications are usually adequate. Cyproheptadine, a histamine-1 receptor antagonist with 5-HT1A and 5-HT2A antagonistic qualities, has been proposed as a serotonin antagonist for the treatment of moderate instances of serotonin syndrome; however, there is little data to support this treatment [11]. Severe, life-threatening cases require immediate attention in the intensive care unit and frequently manifest with hyperthermia (temperature above 41 °C) [11]. In cases of uncertain diagnosis, discontinuation of any serotonergic agents and initiation of supportive care are advisable [12].

3.4. Malignant Catatonia

Multitiered management is necessary for catatonia related to acute medical problems. The goals of treatment should be to address the underlying medical disorders, stop using any drugs that may be perpetuating the disease or causing it, and lessen the catatonic symptoms [32]. Low-dose benzodiazepines (less than eight mg/d of lorazepam) are the major treatment for mitigating catatonic characteristics; results have been observed in 59% to 97% of instances [33]. Other drugs that may be taken into consideration are levodopa, memantine, amantadine, dextromethorphan/quinidine, minocycline, and atypical antipsychotics, even though there is little evidence to support them [32]. Antipsychotic use should be done with caution because reports of malignant catatonia (MC) advancement exist. Immobility and refusal to eat can result in life-threatening medical consequences such as dehydration, pressure ulcers, deep vein thrombosis, or pneumonia [33]. MC patients should get NMS-like therapy, such as dantrolene for severe, intractable stiffness and hyperthermia, as well as short-acting antihypertensive medicines for dysautonomia [32]. Electroconvulsive treatment may be recommended in cases of refractory malignancy. The traditional regimen comprises daily therapy for up to 5 days, followed by three times per week till improvement is achieved [32].

3.5. Status Dystonicus

Status dystonicus is frequently resistant to medications usually used to treat dystonia alone. Treatment of the triggering incident, when possible, is consequently necessary and typically effective. Supportive management, such as that for NMS, is also important. If they do not work, more severe treatment with a combination of high-dose anticholinergics (e.g., trihexyphenidyl), dopamine receptor antagonists (e.g., risperidone), and/or dopamine-depleting drugs (e.g., tetrabenazine) is required. Clonidine, clonazepam, and baclofen may also be effective. Early transfer to an ICU is suggested due to the importance of monitoring respiratory and airway conditions. Some patients may require endotracheal intubation, mechanical ventilation, and sedation with midazolam and propofol [34]. In resistant cases, intrathecal baclofen, pallidotomy, or bilateral deep-brain stimulation of the globus pallidus pars interna may be used [35]. Botulinum toxin is ineffective in the acute situation. Clinicians should be aware that functional dystonia can mirror status dystonicus.

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Therefore, in patients without previous dystonia, doctors should seek favorable signs (e.g., distractibility) of a functional movement disorder [36].

3.6. Myoclonus

Treatment of the underlying disorder is the best therapeutic strategy. Some toxic-metabolic states or surgically resectable lesions can be reversible; similarly, psychogenic jerks can be solved by psychotherapy and pharmacological psychiatric treatment at the first attempt [37]. However, in most cases, multiple drug trials and co-treatment are needed [37]. One useful path to guide treatment is firstly to establish the origin of myoclonus. A gamma-aminobutyric acid (GABA) enhancing or glutamate-lowering approach has historically been of choice given the recognized abnormal excitatory state of the corticospinal output. Although, levetiracetam and piracetam, pyrrolidone derivatives, can be effective in this owing to a different mechanism to modulate cortical hyperexcitability; that is the affinity for synaptic vesicle protein 2A (SV2A) and ions current (i.e., calcium and potassium currents) [38]. Valproic acid remains superior to levetiracetam in cortico-subcortical myoclonus, and it is especially effective in juvenile myoclonic epilepsy (JME) [39]. Brivaracetam has also demonstrated good response rates (up to 75%) as an adjuvant in the treatment of JME. Phenytoin and carbamazepine should also be examined in this scenario. Treatment for subcortical myoclonus, whether nonsegmental or segmental, should be based on the diagnosis. Although some basic recommendations could be made, typical antiseizure medications such as valproic acid and levetiracetam are not consistently effective, although clonazepam, a facilitator of GABAergic transmission, and carbamazepine may be useful at varying amounts. Furthermore, perampanel (an AMPA receptor antagonist) has recently been shown to be useful in treating myoclonus in myoclonus-dystonia syndrome [40].

3.7. Tics

Tics should be treated if they interfere with school or other everyday activities, or that are debilitating due to social embarrassment, physical discomfort, or self-injury. Non-pharmacological therapies include: 1) Behavioral therapy: behavioral therapy has not proven to be very useful for patients with disabling tics. Behavioral methods have included operant conditioning models (rewarding tic suppression and penalizing disruptive tics) and massed practice (repeated, voluntary repetition of a tic until tiredness sets in). 2) If a single tic (or a limited subset of tics) is causing self-injury or discomfort, habit reversal therapy (HRT) should be investigated [41].

When administering tic-suppressing drugs, the medication is normally titrating the dosage until the lowest is found to one that results in disability resolution. When assessing the evidence for the efficacy of tic-suppressing medicines, it is vital to note that a significant placebo response has been recorded [42]. 1) Alpha-2-agonists are moderately effective for tics. Although clonidine was previously the most often utilized alpha agonist, guanfacine is currently preferred since it causes less drowsiness and may usually be dosed once (bedtime) or twice (morning, bedtime), as opposed to clonidine's three to four daily dosages [41]. 2) Dopamine-blocking agents: when an alpha agonist is insufficiently beneficial, the usual supplementation or replacement it with a dopamine receptor blocker. These are the most strong and consistent tic-suppressing drugs. Classical neuroleptic antipsychotics such as haloperidol, pimozide, and fluphenazine have shown efficacy in controlled clinical trials. These pharmaceuticals fell out of favor due to common adverse effects, particularly drowsiness, depression, and mental dulling, as well as the arrival of newer atypical antipsychotic medications. Although it is typically used an atypical antipsychotic (usually risperidone or aripiprazole) as the first dopamine-blocking agent, they are frequently poorly tolerated due to sedation, weight gain, and the development of metabolic syndrome (abdominal obesity, dyslipidemia, hypertension, and impaired glucose metabolism) [41]. 3) Other Tic-Suppressing pharmaceuticals: While alpha agonists and antipsychotics are the most common medications used to treat tics, other types of pharmaceuticals may be beneficial for people who do not respond well or have tolerability issues. In published case series, clonazepam has been shown to have minor tic-

 doi:10.20944/preprints202501.1811.v1

suppressing effects [43]. This medication may be especially beneficial for those with an anxiety problem. It is often used twice or three times daily, with the most common side effects being drowsiness and unsteadiness. Tetrabenazine, a medication that depletes dopamine, may be effective.

3.8. Chorea and Ballism

This disease has no treatment, although the symptoms can be treated. Perhaps most significant is the evaluation and development of a patient support system. As the disease worsens, the patient will require specialized treatment. Nutritional management is critical due to trouble swallowing. Tetrabenazine is licensed to treat chorea [44]. The majority of patients are treated with neuroleptics, which inhibit dopamine receptors. Other medicines include GABAergic compounds such as valproate, clonazepam, and gabapentin. Animal studies have shown potential for both minocycline and CoQ10. Chorea, after a heart transplant, may react to drugs, and plasmapheresis may lessen the duration of chorea in patients with rheumatic fever. Drugs generally only alleviate chorea in a small number of individuals, and they also have serious side effects. Deep brain stimulation (DBS) was developed over the last decade and may aid some chorea patients. Anecdotal evidence suggests that the technique works and lowers chorea in some people. DBS is performed by implanting electrodes in the globus pallidus internus. However, DBS remains an experimental surgical surgery. It does not work for all chorea sufferers and is associated with several problems. Another experimental treatment, neural cell transplantation, has been used to treat a few Huntington chorea patients, but not all have improved [45].

It is critical to treat the underlying cause of hemiballismus, as it tends to resolve over time. As a result, supportive care for comorbidities and associated problems is critical. To treat severe hyperkinetic movements, first and second-generation antidopaminergic drugs that target D2 receptors (e.g., risperidone, haloperidol, perphenazine, pimozide, chlorpromazine), benzodiazepines (clonazepam), anti-epileptics (topiramate), and tetrabenazine are used [46]. If patients are unable to respond to medical treatment and their symptoms are severe enough to interfere with everyday activities, surgery becomes an alternative. The preferred method is a stereotactic posteroventral pallidotomy, which causes decreased firing of pallidal neurons and hence relieves hyperkinetic movements. Microrecording and intraoperative monitoring are used during surgery to increase the precision of the treatment. Intrathecal baclofen has also been demonstrated to be effective in treating post-traumatic hemiballismus [46].

4. Challenges And Considerations

4.1. Diagnostic Challenges

Diagnosing movement disorders can be challenging due to a lack of accurate tests and specialized consultants. Patients admitted to the emergency room are often evaluated by medical professionals who may not be trained to diagnose these conditions. Misdiagnosis of the underlying causes of movement disorders can lead to serious complications, as well as increased mortality and morbidity [47]. Despite the availability of guidelines for the diagnosis and management of movement disorders, many clinicians still face significant challenges in accurately diagnosing these conditions [4].

A prospective study conducted by Dallocchio et al. on 96 subjects with acute movement disorders (MD) showed that chorea was the presenting symptom in one patient with NMDA receptor encephalitis and in two patients with rheumatic chorea. Two patients with a final diagnosis of multiple sclerosis presented with dystonia (right arm) and tremor (left leg) as their first symptoms, respectively. Additionally, one case of acute disseminated encephalomyelitis revealed subacute parkinsonism as the clinical presentation. One patient, who presented with parkinsonism and mild mental confusion, was later virologically confirmed to have HZV encephalitis. They also diagnosed tetanus in two patients who presented with spontaneous and stimulus-induced rigidity. In another case, a patient with a history of HIV infection showed a clinical picture of acute parkinsonism related

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to brain involvement. Additionally, one patient presented with recent limb myoclonus in the context of cognitive impairment and mild ataxia, with a conclusive diagnosis of prion disease. The authors also reported a patient with torticollis associated with a retropharyngeal abscess. Finally, two patients presented with mixed arm tremors and mild myoclonus of the lower extremities, but despite extensive investigations, they did not receive a final diagnosis. This leads us to conclude that many diseases can initially present as movement disorders, even when the final diagnosis is related to another underlying cause, making the diagnosis of movement disorders more challenging [47].

Two case studies of serotonin syndrome were conducted by Mason et al, one case of a 37-year-old woman with symptoms of depression and dysmenorrhea was admitted to Yale New Haven Hospital following a motor vehicle accident. After initial treatment, the consulting psychiatrist started her on valproic acid, clonazepam, and trazodone to manage her depressive symptoms. Ten days after beginning the medication, she began to experience symptoms such as tachycardia, restlessness and generalized confusion. Although serotonin syndrome was suspected at first it is a diagnosis of exclusion and the physicians should conduct all the necessary investigations considering a broad differential diagnosis. In the second case, a 31-year-old man presented with depression following an acute suicide attempt. After receiving appropriate initial treatment, he was started on venlafaxine, taken every 12 hours, one week later. After the first dose, he complained of leg stiffness, diaphoresis, and blurred vision. At the time of consultation, his medications included olanzapine and lorazepam. Following the necessary investigations, all current medications were discontinued, and appropriate emergent treatment was administered. The patient fully recovered the next day. The diagnosis in this case was made based on the abrupt onset of symptoms and the rapid recovery after discontinuation of the medication, despite the broad differential diagnosis for these symptoms [48]. These two case reports emphasize the importance of early recognition of movement disorders in order to perform proper investigations and treatments which can help decrease the morbidity and mortality associated with them.

Patients with neurological disorders can present with symptoms that mimic a stroke, known as stroke mimics. This can lead to unnecessary investigations and the use of thrombolytic therapy [49]. A retrospective case-series study conducted by Hsieh et al. in two-stroke centers in southern Taiwan reviewed stroke code registry data with a final diagnosis of parkinsonism or other movement disorders. Out of seven patients, four had been previously diagnosed with Parkinson's disease (PD), while one was newly diagnosed in this hospitalization. Six of them presented with weakness in the motor function of the limbs. A misdiagnosis of stroke was made in three patients who were evaluated by second-year residents. At the time of discharge, four out of seven patients were diagnosed with PD. One patient was diagnosed with focal left upper limb dystonia, another with myoclonus of the left upper and lower limbs, and one patient with PD was diagnosed with a sleep attack and benzodiazepine overdose. The only patient with a benzodiazepine overdose was treated as having a hyperacute stroke and received intravenous rtPA. However, there were no complications or intracranial hemorrhage [50]. The diagnosis of typical PD with no atypical symptoms is not difficult; however, misdiagnosis in clinical practice is common. Even with available guidelines, 10% of PD cases are misdiagnosed, which is attributed to the overlap between PD and other neurological disorders [51]. A systematic review and meta-analysis included 28 studies conducted by Rizzo et al. Showed that over the last 25 years, the diagnosis of Parkinsonism has been considered challenging. Eight out of ten cases of Parkinsonism receive the correct diagnosis. The accuracy of the diagnosis is influenced by the level of expertise being higher when made by movement disorder experts compared to non-experts. Inadequacy in the diagnosis of PD is more common in the early stages even among movement disorder experts due to the late appearance of most clinical signs. In the early stage, the clinical signs associated with other movement disorders may not appear. Also, elderly patients may have comorbid conditions, leading to more false-positive cases. The duration of the disease is considered a valuable period for achieving an accurate diagnosis. This explains the high diagnostic error in patients with a disease duration of less than five years and the high rate of changes in the initial diagnosis during follow-up [52].

 doi:10.20944/preprints202501.1811.v1

In a population-based study conducted by Schrag et al. on the prevalence of PD, the researchers reviewed registry data of patients diagnosed with PD or other parkinsonian disorders. Out of 202 patients, 134 were diagnosed with PD, including 1 with atypical parkinsonism and 2 with vascular parkinsonism. Additionally, ten patients had been prescribed antiparkinsonian drugs. The onset of tremors was noted in 56 patients after the age of 50, without prior diagnosis, and 2 of these patients were subsequently referred for diagnostic purposes. Out of 131 patients diagnosed with PD, 109 were found to have probable PD. Two patients have possible PD, as their atypical parkinsonism features were not adequate to exclude a PD diagnosis. In 20 of the 131 patients, the diagnosis of PD was invalidated, and these patients were reported to have other movement disorders. Among these 20 patients, 74% reported that their diagnosis of PD had changed during the progression of the disease [53].

This emphasizes the importance of clinical skills for neurologists, especially in the field of movement disorders. Despite advances in neuroimaging and genetics, the diagnosis of PD largely relies on clinical symptoms due to the limited availability of definitive tests. Misdiagnosis is common, particularly in the early stages of the disease, and changes in diagnosis during follow-up are also frequent.

A review study by Kipps et al. reports that NMS is often misdiagnosed as sepsis at the initial presentation, requiring further investigations to reach the correct diagnosis. Additionally, there are many differential diagnoses for NMS, including lethal catatonia, serotonin syndrome, malignant hyperthermia, acute carbon monoxide poisoning, and salicylate, amphetamine, cocaine, and phencyclidine toxicity. In addition, a history of exposure to one or more serotonergic drugs makes the distinction between NMS and SS more difficult. However, the presence of myoclonus, seizures, and hyperreflexia, along with clinical symptoms, tends to favor a diagnosis of SS [54].

A prospective study conducted by Dallocchio et al. on 96 subjects with acute movement disorders (MD), emphasized that the second most common acute movement disorder is functional movement disorder (FMD). Patients with functional movement disorder are often referred to the ED for diagnosis, and it is difficult to distinguish it from acute movement disorder. This challenge arises because all patients with acute movement disorder can also exhibit psychiatric and functional disorders, accounting for 19.8% of the presentations. Among these patients, 5 out of 19 have comorbid psychiatric conditions [47]. This leads us to conclude that there is a relationship between movement disorders and psychiatric disorders.

Patients with PD can experience acute psychosis parkinsonism, which may be triggered by environmental changes. This psychosis can result from an infection or the recent introduction of a new medication, especially if the medication is a dopamine agonist, anticholinergic drug, amantadine, or catechol-o-methyltransferase (COMT) inhibitor. Symptoms of psychosis in PD include delusions and hallucinations. The diagnosis of acute psychosis in PD relies on excluding other metabolic disorders and assessing for underlying psychiatric conditions, such as depression [54]. Psychosis is common in PD and is associated with increased morbidity and reduced quality of life. Early diagnosis and management are important to mitigate medication side effects that can worsen the symptoms [55].

4.2. Treatment Challenges

Dantrolene sodium is approved by the U.S. Food and Drug Administration for use in neurology and anesthesiology for both adults and children. Its primary indication is the treatment of malignant hyperthermia. Dantrolene is also used in cases of NMS due to the similarity in presentation to malignant hyperthermia. However, dantrolene is associated with adverse effects, including muscle weakness, which can affect both skeletal and respiratory muscles, leading to a decrease in respiratory capacity. Dantrolene is rarely associated with liver injury, which may occur due to the formation of toxic metabolites such as acetylamino-dantrolene and hydroxylamine. Liver function test should be done in case of chronic use [56]. Dantrolene has been reported to cause phlebitis at the injection site, along with drowsiness and confusion. In cases of chronic use, it may rarely lead to gastrointestinal

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symptoms and visual disturbances. Dantrolene has been observed to cause prolonged recovery time when taken in combination with non-depolarizing neuromuscular blockers [57].

The primary effects of benzodiazepines are sedation and the reduction of anxiety and agitation. However, benzodiazepines have also been reported to cause aggressive behavior symptoms after use. Benzodiazepines are also associated with dependency, particularly in the elderly, as well as tranquilizing, cognitive, and psychomotor effects. Precautions should be taken during the withdrawal of the drug, as it is associated with serious complications [58]. Benzodiazepines can cause amnesic effects, including difficulty in acquiring new information and problems with information storage [59]. Various studies have reported an increased incidence of falls in older adults who use benzodiazepines [60]. The most severe withdrawal symptoms of benzodiazepine occur 8 days after drug cessation. Diazepam is associated with seizures arising 21 days after discontinuation [61].

Anticholinergic drugs work by blocking the muscarinic receptors and inhibiting the cholinergic function. This mechanism leads to wide peripheral effects and also central effects are observed, such as confusion and disorientation [62]. Anticholinergic drugs are widely used drugs. It is used to treat movement disorders, such as status dystonicus. However, they have been reported to cause numerous unwanted side effects, such as cognitive impairment. Recent studies on elderly patients have emphasized the effects of anticholinergic medication use, suggesting a strong association between anticholinergic medication burden and cognitive decline and dementia [63]. The cognitive dysfunction, mainly memory impairment, results from the action of anticholinergic drugs at M1 receptors, antagonizing its function and, to some extent, M2 or M4 receptors in the central nervous system. Although anticholinergic drugs lead to cognitive impairment, this effect is associated with the drug's ability to penetrate the blood-brain barrier (BBB) and act centrally [62].

The elderly population is more sensitive to the adverse effects of anticholinergics, which can lead to cognitive impairment. It has been reported that older Americans prescribed at least one type of anticholinergic medication may develop cognitive dysfunction [64]. The adverse effects are especially notable with high doses of anticholinergics. A dose-response association has been observed between anticholinergic use and an increased risk of dementia. Current evidence suggests that regularly monitoring the anticholinergic load before prescribing these drugs can help reduce anticholinergic-related side effects in older adults [65]. A systematic review study conducted by Stewart et al. reported associations between anticholinergic burden and physical function, as well as quality of life in the elderly [66]. Anticholinergic agents may also influence the timing of the onset of psychotic symptoms in patients with Alzheimer's disease [67]. A cross-sectional study conducted by Wilczyński et al. in geriatric hospitals found that 40.73% of patients were burdened with at least one anticholinergic drug, and 13.98% reported experiencing a significant burden from these medications [68].

Various anticonvulsant drugs are currently available for the treatment of seizures and movement disorder emergencies; however, they are associated with a spectrum of side effects, ranging from acute to chronic [69]. Antiseizure medications have been reported to cause uncontrolled and breakthrough seizures, severe dose-dependent side effects, long-term toxicity, and interactions with other medications [70]. A case report of a 52-year-old man who came to the emergency department with multi-organ failure due to Valproic Acid Toxicity [71]. Some antiseizure medications, such as valproic acid, lamotrigine, and phenytoin, can lead to the formation of reactive metabolites, including arene oxide, N-desmethyldiazepam, 2-(1-hydroxyethyl)-2-methyl succinimide, 2-(sulphamoylacetyl)-phenol, E−2-en-VPA, 4-en-VPA, and carbamazepine-10,11-epoxide. These metabolites are associated with wide adverse effects, including hepatic injury, birth defects, and cutaneous hypersensitivity. Patients with a history of hypomania are likely to experience a recurrence when taking gabapentin. It is also associated with aggressive behavior and irritability and may worsen seizure symptoms due to its psychiatric effects. For these reasons, gabapentin is not currently used in children [72]. The anticonvulsant felbamate has been reported to cause aplastic anemia, with an incidence of approximately 127 cases per million. It can also cause hepatic injury. Dermatological side effects have been widely reported with antiseizure medications, with

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lamotrigine being commonly associated with serious rashes, including SCARs. These rashes may occur due to risk factors such as starting with a higher-than-recommended dose, concurrent use of valproate, and a history of rashes caused by anticonvulsant drugs. Other antiseizure medications, such as carbamazepine, phenobarbital, and phenytoin, are also linked to serious dermatological conditions, including SJS [73]. For status epilepticus, phenytoin is used as a second-line treatment. Intravenous fosphenytoin, a prodrug of phenytoin, is the recommended option since it has fewer negative effects than phenytoin. However, the use of fosphenytoin can result in serious adverse effects, such as hypotension, arrhythmia, and allergic reactions. During these situations, it is important to maintain respiratory and circulatory function. Elderly patients or those with a history of heart problems are especially at risk [74].

Phenytoin is also thought to cause other side effects, including vein irritation, alkalinity of the vehicle, hypotension, and "purple glove syndrome" (PGS), which is a condition where drug extravasation causes distal limb edema, discoloration, and pain. Propylene glycol, the vehicle used in parenteral phenytoin, has the potential to be toxic to the kidneys and heart. Intravenous phenytoin is considered one of the main therapies for status epilepticus, even though it isn't considered the first-choice agent [75].

Levodopa treatment has been proven to alleviate PD symptoms. However, it became evident in the late 1960s that a significant number of levodopa-responsive patients experienced dyskinesias and motor fluctuations as side effects. After 4-6 years of levodopa medication, 40–75% of individuals developed these side effects. Recent studies have reported that the clinical duration of levodopa's effectiveness can vary with respect to both motor and non-motor symptoms [76]. The motor symptoms include dyskinesias. The dyskinesias are usually associated with maximal improvement in motor response and high plasma concentrations of levodopa (peak-dose dyskinesia). These dyskinesias can present as dystonia, choreiform movements, or other movement abnormalities. Dyskinesias that occur at or shortly before the start of the "on" response, disappear during the "on" period and then reappear as the 'off' phase starts are less common (diphasic dyskinesias). PD patients may also experience off-period dystonia, which occurs in their legs and is frequently accompanied by pain and a persistently abnormal posture [77]. A prospective study showed that all the patients with motor dysfunction are reported to have non-motor dysfunction, including dysautonomic fluctuations, mental fluctuations, and sensory fluctuations [78]. The majority of non-motor fluctuations (NMF), including anxiety or impaired thinking, were linked to the 'off' state. However, 36% of patients reported hyperactivity and 42% reported euphoria, all of which occurred during the 'on' or pre-'on' stage. A high motor score was directly associated with the total number of NMFs reported by each patient, but not with the dosage or duration of dopaminergic treatment [79].

4.3. Ethical Considerations

The concept of informed consent has been established for a long time and has gradually gained recognition. In the last century, it has been a legal and ethical principle in medical practice and research [80]. There are two fundamental principles of informed consent. First, the doctor must provide adequate information regarding the patient's case. Second, patients have the right to make decisions about what will be done with their bodies [81]. Informed consent is widely accepted in the United States. However, in other communities, it is influenced by cultural diversity, where many people rely on their families and communities when making important decisions [80]. For consent to be valid, the patient must have the mental capacity to understand the medical information and the consequences associated with the intervention decision as well as the ability to make medical decisions [81]. In the setting of neurological diseases, many patients may lose the ability to make decisions as a consequence of neurological degeneration and cognitive impairment which affects the patient's autonomy making it difficult to assess their competence [82]. It is well recognized that in Huntington's Disease (HD), psychiatric and cognitive impairments lead to the deterioration of mental functions. This has a significant impact on the quality of life and daily activities [83]. In the context of neurological diseases where patients have impaired cognitive and decision-making abilities, the

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patient does not lose the right to decide whether to accept or refuse treatment. In such cases, the decision is delegated to a surrogate who has the right to consent or refuse treatment on the patient's behalf [84]. The physician should explain to the surrogate of incompetent patients the same information as provided to competent patients and obtain consent for treatment and investigations [84]. The assignment of surrogate decision-makers can be either formal or informal. Formal assignments are established through advance directive statutes, such as Durable Power of Attorney for Healthcare, which allow individuals to designate formal surrogates when they were competent. For patients without families, government agencies assign legal representatives to make decisions on their behalf [84]. Physicians should provide information without bias. Although it may be challenging for a physician to remain unbiased due to their knowledge of which treatment is better and why, there is a distinction between opinion and fact. Physicians should explain their opinions about the treatment options and the rationale behind them. Patients should receive objective information to assist them in making informed decisions [84]. Autonomy and beneficence are interconnected, but this relationship can be overlooked in the context of neurological diseases where patients may be unable to determine what is best for themselves. In such cases, surrogates should be well-informed about the patient's wishes [85]. There are challenges related to informed consent, such as physicians not receiving adequate training in practice and frequently misunderstanding legal standards. Additionally, patients often have limited knowledge about alternative treatment options [80] and also an inefficient understanding of informed consent among patients regarding various aspects. This may be attributed to the lack of adequate time for comprehension between physicians and patients. Additionally, emotional factors may affect patients' knowledge about the risk factors of surgical procedures, contributing to a suboptimal understanding [86]. Since few effective therapies exist for neurological diseases, the physician should explain the genetic test in detail, including how it can positively affect the management of patients [82].

There is no specific time to begin end-of-life care; it can start when needed. The timing varies according to the health system, ranging from hours to days before death. Specialized care for the dying can be provided as part of end-of-life care for months [87].

In the context of neurological diseases like HD and Alzheimer's disease, early discussions about end-of-life care are essential. As these diseases progress, patients lose the ability to make decisions and communicate effectively. Early planning helps reduce unnecessary treatments and hospitalizations in the future [88]. in neurological disease, Physicians should utilize the period following diagnosis to discuss end-of-life care as the time between diagnosis and the loss of patient autonomy may be limited. Therefore, physicians should make the most of this period and avoid wasting it [89]. Accurate prognosis in neurological diseases is often not possible due to the lack of comprehensive data. Even patients with an initial Glasgow Coma Score of 3 can recover and interventions in neurological diseases carry the risk of severe complications [85]. The unpredictable course of neurological diseases can also represent a challenge in starting end-of-life care [88]. End-of-life care in India faces more challenges compared to developed countries. This may be attributed to ethical and cultural diversity, as well as a stronger emotional connection with family and friends, along with greater support from families [88]. Most patients with serious long-term neurological diseases and limited treatment options need guidance on how to live their lives before death. This can be addressed through a specialized medical approach called palliative care [90]. Palliative care is "an approach that improves the quality of life of patients and their families facing problems associated with life-limiting illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual (palliative care, WHO)." A study conducted in India by Gursahani et al. reported that There are only 200 trained palliative care specialists, and most of them work primarily in the field of oncology. Additionally, most physicians are not trained to address the complexities of palliative care discussions [89]. Studies have shown that patients with PD experience similar end-of-life suffering as those with end-stage cancer. However, they do not receive the necessary attention and care. This highlights the urgent need to increase awareness about palliative care for PD patients

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[91]. Hospice care provides specialized care for patients expected to die within six months. Discussing hospice care is a sensitive issue, as it signifies that curative treatments are no longer beneficial [90]. It is evident that patients with neurological diseases suffer as the disease progresses, and they require more attention regarding their end-of-life care needs. Before patients lose their autonomy, early discussions can help them maximize the benefits of this care and avoid unnecessary treatments. Specialized training for neurologists is also essential.

5. Future Directions and Research Needs

As the disease progresses patients with movement disorders, including PD will eventually develop disability despite the symptomatic treatments available. Most treatments for PD focus on restoring dopamine (DA) levels through the administration of the DA precursor levodopa or DA agonists. However, over time, the therapeutic window of these drugs narrows, leading to decreased efficacy. Additionally, many of these treatments are associated with side effects such as dyskinesia and hallucinations [92]. In spite of recent advancements in the pathogenesis and treatment of movement disorders such as PD, many of these diseases remain difficult to diagnose and treat. Therapies targeting disease progression often fail to achieve their intended goals. Continued study of the pathophysiology of these disorders and translating research findings into the development of new therapeutic agents will lead to better outcomes [93]. Significant advancements have also been made in clinical work on parkinsonism, HD, essential tremor, and tic disorders [93]. Clinical trials conducted in the past 5 to 10 years have selected candidates based on preclinical models but have not adequately addressed the heterogeneity of PD subgroups [94]. Lysosomal dysfunction may be a prominent and early stage, but many factors that affect the management outcomes should be addressed [95]. The same applies to HD; current treatments aim to improve the quality of life and address motor, cognitive, and psychiatric symptoms. This highlights the urgent need to develop new treatments to alter the disease course. A lot of clinical trials have been conducted, but none of these experiments have succeeded in providing treatments that affect disease progression despite some of these trials showing positive results in preclinical studies [96].

The key role in PD pathology is lysosomal dysfunction, with a high prevalence in GBA1, which encodes the lysosomal enzyme glucocerebrosidase. This defect leads to the pathological accumulation of alpha-synuclein a major component of Lewy body intracellular aggregates, resulting in inflammation in the nervous system and neuronal dysfunction. Based on this information, Abeliovich et al. conducted a study to emphasize the need to develop gene therapy aimed at delivering the GBA1 gene for PD-GBA. The investigational drug PR001 represents the first clinical stage and adeno-associated virus serotype 9 (AAV9) as the vector [97]. The selection of AAV9 is due to its efficient brain transduction and safety profile in humans [98]. A lot of therapeutics for PD are under evaluation. These agents can be categorized according to their specific molecular targets to anti-α-synuclein antibodies: monoclonal antibodies targeting α-synuclein in different regions to enhance its clearance while blocking its adverse cellular effects on neurons, ultimately reducing toxicity and pathological spread [94]. Currently, available treatments include active immunization with vaccines (PD01A and PD03A) and passive immunization with antibodies (BIIB054, BAN0805, PRX002, also known as RO7046015, MEDI1341, and AF82422) [99,100]. The second drug is LRRK2 inhibitors, which target the LRRK2 pathway, the most common cause of autosomal dominant PD that leads to a gain of toxic function and enhanced propagation of α-synuclein. These inhibitors have been developed and have shown significant benefits in preventing neurodegeneration [94]. The third drug, Ambroxol, works by enhancing the translocation of mutant β-glucocerebrosidase, which leads to increased β-glucocerebrosidase activity in cells carrying GBA mutations [101].

New technologies have been discovered using embryonic stem cells (ESCs). Stem cell transplantation can provide a solution to the potential problems associated with fetal DA precursor cell transplantation. Fetal human neural stem cells (hNSC) are considered the earliest, uncommitted multipotent cells of the central nervous system and can differentiate into more specialized neural cells. Studies have shown that grafted fetal human neural stem cells (hNSCs) can give rise to new

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neurons and glial cells and integrate within the degenerative brain. However, the differentiation of these cells into the appropriate dopaminergic (DA) neurons, whether in vitro or after in vivo after transplantation, has been demonstrated to be inefficient. This highlights the need for methods to convert stem cells into midbrain-subtype DA neurons before transplantation to make this approach a viable clinical option [92].

Gene therapy using viral vectors is now considered one of the treatments for PD. Viral vector allows the delivery of specific genes at different neuroanatomical loci and requires one intervention to provide long-term therapeutic effect giving it more advantages than pharmacotherapy [102].

6. Conclusions

Patients presenting in the ED with movement disorders should first be assessed regarding airway protection, and the ED physician needs to describe the movement in detail for a precise diagnosis. The description of the phenomenology facilitates the general neurology consultant's ability to provide a better plan. After the general description, the ED physician should focus on the basic guidelines for managing every movement disorder. A common question for all the patients presenting in the ED would be regarding recent medications started or dose changes; after that, a basic comprehensive metabolic panel can elucidate the diagnosis of most pathologies.

Author Contributions: J.P.R., I.K., A.F.G., O.D.M., M.Y.E., R.S. and A.L.F.C. conceived and designed the methodology of the literature review. J.P.R., I.K., A.F.G., O.D.M., M.Y.E., and R.S. extracted and collected the relevant information and drafted the manuscript. A.L.F.C. supervised the article selection and reviewed and edited the manuscript. J.P.R. and A.L.F.C. reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data was created.

Acknowledgments: None.

Conflicts of Interest: The authors declare no conflicts of interest.

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