

Review Article

Movement Disorders: Recognition, Diagnosis, and Challenges in Care Delivery Pathways Involving the Primary Care and Specialist in Community Health Setting

Vadiee M*

Fellowship Candidate Parkinson's Clinic Dept Neurology Baylor College of Medicine, USA; Senior Reviewer for American Journal of Geriatrics & Gerontology; Postdoctoral Chronic Care Medicine, Queen Mary University London, United Kingdom; Assistant Professor Internal Medicine Geriatrics & Gerontology International Program, Jagiellonian Medical College, Poland; Assistant Professor Institute of Public Health European Public Health Program, Jagiellonian Medical College, Poland

***Corresponding author:** Massod Vadiee, Fellowship Candidate Parkinson's Clinic Dept Neurology Baylor College of Medicine, USA; Senior Reviewer for American Journal of Geriatrics & Gerontology; Postdoctoral Chronic Care Medicine, Queen Mary University London, United Kingdom; Assistant Professor Internal Medicine Geriatrics & Gerontology International Program, Jagiellonian Medical College, Poland; Assistant Professor Institute of Public Health European Public Health Program, Jagiellonian Medical College, Poland

Received: May 12, 2020; **Accepted:** June 04, 2020;

Published: June 11, 2020

Abstract

The movement disorders are chronic neurodegenerative group of diseases such as; Parkinson's disease, Huntington's disease, tremor, and dystonia which are increasingly becoming more prevalent. The establishing of their classification, accurate diagnosis and clinical management can be a difficult and lengthy process in part due to their complex natural history and heterogeneous presentations. Unfortunately, the under recognition and under diagnosed movement disorders are also common partly as a result of the clinicians inadequate understanding of disease phenomenology and phenotypical variability and challenges related inability to differentiate functional and secondary movement disorders from organic movement disorders. In addition to challenges of clinicians knowledge and attitudes and the lack of coordination and obstacles in the dynamics of care pathways that link the primary care services with the higher specialists care can significant have adverse impacts on of quality of the chronic neurological care delivery needed among the vulnerable patient population. A unique group of conditions that are commonly encountered by the community healthcare providers are the secondary movement disorders or the mimickers of movement disorders that include the drug-induced and the systemic or metabolically-induced movement disorders which present both as a diagnostic and management challenge and opportunity for the general practitioners and community neurologist alike.

Keywords: Movement disorders; Chronic neurological care; Clinicians knowledge and attitudes; Healthcare delivery primary care; Secondary movement disorders; Drug and metabolically -induced movement disorders

Overview

The management of patients with movement disorders require an integrated and responsive service that can provide accurate diagnosis, appropriate treatment, a sustained long term care and if needed timely referral. With increasing aging population and the inadequate access to chronic neurological care, novel care delivery approaches are needed. The principal component of any quality healthcare system is the timely access to a patient-centered care and this may vary considerably depending on the type of care sought, patient populations profile the geography. The failure to accurately diagnose neurological conditions may result in delayed treatment and patient's unnecessary loss of daily function and productivity. The complex interface of care pathways between patient's point of contact with the primary care settings and the complementary care services including neuropsychiatry, neuroradiology, palliative care, physiotherapy and rehabilitations are also either not optimized or unable to meet patient's needs and expectations. The availability of a sustained chronic care among patients Parkinson's, tremors and dystonias and other with movement disorders is fundamental and currently, limited data is available on the level of integration and coordination that is embedded in our care pathways and in particular between rural community practitioners and the specialist care. Surprisingly, in comparison with other medical disciplines and specialties, the specialized neurological

care particularly at the community level appears to be least integrated into the overall healthcare delivery system. With respect to the movement disorders there is an urgent need for innovative approach in delivery and service utilization to address the current gaps and ensure truly patient-centered outcomes. For majority patients living with movement disorders such as Parkinson's, Dystonia, Tremors and other forms of chronic neurological conditions the access to primary care for initial clinical assessment and referral to specialist is essential. Moreover the clinicians interpretations of patient chief complaints, history, clinical examination and the ability to distinguish and differentiate functional and secondary movement disorders from organic in movement disorders requires a considerable clinical knowledge and diagnostics acumen. This transition from primary to secondary care pathway services can be a costly and stressful experience for patients, while the outcomes can vary with practitioner's knowledge, attitudes, and the availability of coordinated care between primary and tertiary specialized centers. For a favorable management of movement disorders, a focused initial assessment of patient's early clinical presentations by the primary care team and a timely referral for further investigations can have a major impact on disease progression and eventual outcome. Currently, no clear policy exists on the preferred pathway of care and the extent by which the primary care sector should be involved in management of patients with movement disorders and chronic neurological conditions.

Key Points

- Establishing classification and understanding phenomenology are crucial in arriving at a diagnosis of movement disorders. The phenomenology is determined from the specific combination of the dominant movement disorder (akinetic-rigid and hyperkinetic) and presence of additional neurological or non-neurological abnormalities.
- A systematic approach is recommended when approaching patients with movement disorders. The drug and metabolically – induced movement disorders as mimickers that are commonly encountered in community healthcare setting and provide an opportunity for the skilled general practitioners' to evaluate before proceeding to seek second opinion and specialist referrals.
- To ensure optimal clinical outcome and a patient-centered care patients we should foster clinicians enhanced knowledge and attitudes and scale up coordinated care pathways that link the primary and the higher specialist care levels into the overall ecology of long term chronic neurology services.

Method

We decided to use a mini-review to search of literatures in order to uncover the novel causal factors that exist between the classifications and diagnostics aspect of chronic neurological care. In particular, with regards to the movement disorders we were also interested in the exhibiting literatures on topics related to clinician's knowledge and attitudes, the neurological are integration into primary care pathway. We intended to explore and describe the challenges related to possible neurological service gaps experienced by patients when navigating between general practitioners and specialist neurologist services in the community healthcare setting. We performed a pubmed search of published literature from 2015 to 2015. The key search terms included; neurological care, movement disorders, primary care, neurology specialist referral practitioners' knowledge and attitude. We also performed a second literatures search for publications that had addressed the non-neurological secondary movement disorders such as; systemic and metabolic-induced and or drug-induced movement disorders commonly encountered by community neurologist and general practitioner in primary healthcare centers.

Challenges of classifications and understanding phenomenology

Movement disorders (i.e.; Parkinson's disease, tremor, Huntington's disease dystonia, myoclonus, tics, etc) are a related group of neurological conditions that previously referred to as 'extrapyramidal disorders' and anatomically originate from basal ganglia, although clinical phenomenology plays a more important role than anatomic location in classification and diagnostic schemes. These abnormal movements maybe voluntary or involuntary and categorized as either hyperkinetic or hypokinetic voluntary and automatic movements that are not unrelated to weakness or spasticity. The movement disorders furthermore can be categorized as either primary, or secondary depending on the underlying cause, with primary movement disorders the abnormal movement considered as the primary manifestation of the disorder, while in secondary movement disorders, a broader systemic, structural, metabolic, toxic or inherited factor might be the etiological culprit [1,2]. Currently,

biological investigations on animal models have shown insights into the pathophysiology of movement disorders and understating of the natural history of movement disorders and other neurodegenerative conditions. Currently, the clinical examinations based on our understanding the phenomenology of the abnormal movement are the pillars of our diagnostic approach, and the therapeutic management remain largely symptomatic with select cases the radio-surgery and deep brain stimulation have shown some promising results [2-4].

The epidemiological studies show that a fifth of all movement disorders were diagnosed to be probably drug-induced, and Parkinsonism and increasing trend in clinical burden indicates a need for increased resource allocation, education and training meet the increased demand for movement disorders specialist as community neurology practitioners in resource limited community healthcare settings [5-7]. The Parkinson's disease and other common movement disorders are usually neurodegenerative progressive, dsabling conditions and associated significant economical burden and reduction of patients daily activity and quality of life. The symptomology are not exclusively motor but also non motor features (i.e.; sialorhea) with psychiatric sequel which are stigmatizing impairing patients emotional well-being and can exert substantial economic burden on patient and caregivers [8-10]. The general classification of movement disorders is a complex and diagnostic task is often compounded by its clinical phenotypic variability. Nonetheless, attention to pattern recognition such as; akinetic-rigid, or hyperkinetic movements or presence or absence of jerky character will often lead the clinician to diagnosis of movement disorders. Although the complex and mixed-patterns movement disorders require a sophisticated understanding the phenomenology of the clinical syndrome, and additional systematic search for presence of dominant abnormal movement in conjunction with neurological or non-neurological presentations are required in order to arrive at a an accurate diagnosis [11,12]. WITH the clinical heterogeneity and phenotypic diversity that is commonly observed among patients with movement disorders the diagnostic value of a detailed systematic approach is quite justifiable. The search for phenomenology of the movement disorders is grounded in an age appropriate focused clinical examination and relevant information on quality of disease onset, progression, and possibility of existing drug toxicity [12,13].

The classification and categorizing movement disorder patients can be cumbersome task using current diagnostic criteria without additional neuro-pathological and psychiatric investigations. Therefore, detailed examination and lengthier clinical investigations are often needed in order to accurately differentiate between patients who might represent an atypical presentations of movement disorder or those who indicate a population that is concurrently unrecognized or under-diagnosed [14,15]. A large cohort study of patients with Parkinsonism showed that 74.7%, were drug-induced Parkinsonism followed by vascular parkinsonism other rare sporadic, genetic, infectious etiologies [16-18]. Therefore in the absence of a biologically meaningful biomarkers or reliable gold standard test it is of paramount importance to anticipate the prodromal phase of movement disorders either with motor, no-motor or cognitive symptoms among patients with atypical variant of Parkinson's disease and ensure early accurate diagnosis [17-20].

A number of studies illustrate that with regards to the

management of movement disorders, adhering to diagnostic criteria and timely recognition of prodromal clinical signs and symptoms can potentially yield moderate to high predictive power of the likelihood for an earlier diagnosis, adequate neuro-cognitive support and timely referral and facilitations for long term care planning [21-25]. A coordinated service delivery service link between the primary care physicians and higher specialist neurologists would allow a systematic and comprehensive evaluation of patients that could investigate memory, cognitive, perceptual-motor as well as balance and gait. This requires a reform in the manner by which [24-26]. The new data and technology driven neuro-radiological diagnostics and artificial intelligence have inspired new pathways of delivering chronic neurological care and also opportunities for novel practice of neurology as a discipline [27-29]. Additional challenges continue to exist with respect to the traditional medical education curriculum and its failure to adequately train and sensitize a more knowledgeable generation of residents and community based neurology practitioners that can manage patients with movement disorders and other long term neurological conditions [30-33].

Movement disorders mimickers: drug induced and neuro-metabolic movement disorders

A wide range of conditions, both neurological and non-neurological can mimic various movement disorders, therefore it is vital for the clinicians to systematically approach patients who present with one or more types of movement disorder. Among the diverse movement disorders, the secondary dystonias, and dystonic movements are a good illustrations of pathophysiological and genetic heterogeneity associated with secondary movement disorders and may etiologically be associated with exogenous processes including focal and diffuse neuronal damage, impaired systemic metabolism, dysregulation noxious substances, and toxic effects of therapeutics drugs that invariably can lead to a pathological process known as oligonucleotid repeats processes [34,45]. The heterogenic etiological nature of movement disorders like pseudo-dystonias or psychogenic dystonia require a broader knowledge of natural history of these conditions and a clinical precision in establishing the differential diagnosis to successfully recognize and diagnose different clinical scenarios [34-36].

The current research on phenomenology and clinical presentations of movement disorders (Parkinson's disease, Dystonia, tremors; etc) indicate that they commonly precede with nonspecific symptom presentations that include; tremor, memory and cognitive decline depression fatigue, dizziness, urinary dysfunction, sialorhea, constipation and gait and balance abnormalities.. Therefore a robust clinical knowledge and a judicial anticipations of nonspecific presentations early in the course of the disease by the primary care physicians is essential for earlier diagnosis and referrals [37-40]. While in Parkinson's disease and other movement disorders the core etiologies are vascular infections, and or space-occupying lesions, with secondary movement disorders the underlying cause maybe psychogenic and drug induced which often missed or under-recognized by the primacy providers [39,40]. The psychogenic movement disorders as mimickers of organic movement disorders present with normal laboratory and imaging tests and routinely exhibit bizarre gaits, tremor, dystonios, myoclonusparoxysmal dyskinesias and jerkiness that could involve face, neck, trunk or limbs

but the diagnosis is based on paroxysmal nature and variability of tremor direction, and swaying gait and balance without falling [41-43].

The drug-induced movement disorders are commonly the result of dopamine receptor-blocking agents (Levodopa neuroleptics, calcium channel blockers, illicit drugs) causing dyskinesias dystonia, hyperkinetic or hypokinetic movement disorders. With the aging populations and higher rate of comorbidity and polypharmacy the potential risk of drug-induced movement disorders among the elderly requires for a careful risk assessment and a comprehensive review of current medications by primary care physicians should be of considerations [44-46]. Another group of therapeutics that precipitate drug-induced movement disorders are antipsychotics, antiepileptics, antimicrobials, antiarrhythmics, gastrointestinal drugs that are causative agents for parkinsonism and the extrapyramidal side effects such as tremor, chorea-ballismus, dystonia, tardive dyskinesia, myoclonus, and tics [46-48]. The drug-induced movement disorders are among the most commonly encountered and at the same time under-recognized conditions by the primary practitioners, with the younger patients typically presenting with acute presentations and elderly exhibiting tardive or subclinical Parkinsonism. In the absence of a definitive laboratory and imaging tests for movement disorders, the clinicians awareness of clinical presentation, knowledge of risk populations and the ability to distinguish the drug-induced Parkinsonism from Parkinson's disease remains a challenge particularly in the communities with limited access to higher levels of care pathways and [49-52].

The hepatics and metabolically-induced -movement disorders

Movement disorders may also be under recognized when arising in the context of systemic disease and metabolic disorders. Abnormal movements may be the initial manifestation of a systemic disease, with the pro-inflammatory mediators and microglia acting as triggers that accelerating metabolic and biochemical dysregulations in the central nervous system [53,54,66]. Therefore ascertaining movement phenomenology with acute or sub-acute presentations and unexplained prodromal clinical and psychiatric symptoms might suggest that a systemic process such as metabolic, endocrine infectious, autoimmune diseases might be the underlying cause of the movement disorders [54-56]. The movement disorders arising in the context of a broad range of metabolic disorders or inborn errors of metabolism present with acute and sub-acute ataxia, hyperkinetic, hypokinetic or rigid movement syndrome. Among the systemic metabolic syndromes, the cardiovascular and the diabetes mellitus Type 2 disease are known as risk factors for secondary movement disorder as these metabolic syndromes compromise neuronal function due to hyperglycemic and pro-oxidative states undermine neuronal protection which lead to unique movement disorders [57-59]. The current research evidence increasingly point to the brain-gut microbiotic axis and the role that the gut innate immune system might have as a result of up-regulation of inflammatory cascades and enteric neuroglial cells that hinder the neuronal protection in genesis of the motor and cognitive symptoms among patients with Parkinson and other progressive movement disorders [60, 61].

The dystonias are among the movement disorders that frequently

can be the manifestation of neurometabolic conditions that clinically present with paroxysmal onset orofacial movements involvement with associated neurological and extra-neurological features that can prompt the clinician to consider a more diligent history and a particular attention to phenotypical presentation of the particular movement disorder [62-64]. The underlying pathophysiological cause of neurometabolically induced movement disorders broadly associated with hepatic syndromes role in causing mitochondrial cytopathies organic acidurias, purine-creatine metabolism and lipid storage disease that lead to permeability of the blood-brain barrier and neuroinflammatory induction of circulating cytokines encountered in hepatic encephalopathy, myelopathy, and cirrhosis-related parkinsonism [65-67]. Finally, in the Wilson disease as an inherited metabolic disease causing excess copper buildup can cause a distinct category of neurodegenerative abnormal movement disorders that in clinically may present with chorea, dystonia, myoclonus, tremor, and parkinsonism in children, while on the other hand the inborn abnormal iron deposition also with genetic etiology can present with extrapyramidal movement disorder without intellectual disability disorders [68-71]. A timely recognition and characterization of these secondary movement disorders in the context of age of onset and clinical presentation is essential and requires addressing the underlying neurometabolic disorder [72-74].

Conclusion

The movement disorders are a group of chronic neurodegenerative conditions that increasingly are becoming more prevalent and continue to be a considerable economical burden on healthcare system. The establishing of classification and an accurate diagnosis of movement disorders can be a difficult process in part due to complex and heterogeneous presentations and its natural history. There are indications that among underserved populations such as elderly with less access to specialized neurological care in general the chronic neurological conditions and specifically the movement disorders are unrecognized or under-diagnosed. The complex interface of care pathways often lack integration and the an optimal management, treatment and continuous and coordinated care for patients with movement disorders remains a challenging task as it and as it requires not only a well trained knowledgeable and sensitized primary care team but also a cross disciplinary care pathway that is capable of providing timely evaluation and specialist referral. A unique group of conditions that are neurological and non-neurological that mimic various movement disorders and are either the drug or metabolically-induced movement disorders are commonly encountered in community healthcare setting, providing both a challenge and an opportunity for general practitioners' to evaluate and potentially manage before referrals. More research is needed to explore the current extent and availability of coordinated care that exists between primary and higher specialist care for a sustainable care aimed at patient with movement disorders. Moreover, an innovative approach is vital for novel approaches into the organization and integration of community neurology services and into the overall ecology of the healthcare system.

Additional Reading Sources

1. Fahn S. Classification of movement disorders. *Movement Disorders*. 2011; 26: 947-957.

2. World Health Organization. Neurological disorders: public health challenges.
3. World Health Organization. Atlas: country resources for neurological disorders. 2004.
4. Obeso JA. Past, Present, and Future of Parkinson's Disease: A Special Essay on the 200th Anniversary of the Shaking Palsy. *Movement Disorders*. 2017; 32: 9.

References

1. Lanska DJ. Chapter 33: The history of movement disorders. *Handb Clin Neurol*. 2010; 95: 501-546.
2. Haunton VJ. Movement disorders: a themed collection. *Age Ageing*. 2019; 49: 12-15.
3. Picillo M, Munhoz RP. Medical Management of Movement Disorders. *Prog Neurol Surg*. 2018; 33: 41-49.
4. Béreau M, Tranchant C. Les mouvements anormaux: mise au point [Movement disorders: An update]. *Rev Med Interne*. 2018; 39: 641-649.
5. Wenning GK, Kiechl S, Seppi K. Prevalence of movement disorders in men and women aged 50-89 years (Bruneck Study cohort): a population-based study. *Lancet Neurol*. 2005; 4: 815-820.
6. Louis ED, Ferreira JJ. How common is the most common adult movement disorder? Update on the worldwide prevalence of essential tremor. *Mov Disord*. 2010; 25: 534-541.
7. Eu KM, Tan LC, Tan AR. Spectrum and burden of movement disorder conditions in a tertiary movement disorders centre--a 10-year trend. *Ann Acad Med Singapore*. 2014; 43: 203-208.
8. Martinez-Martin P, Macaulay D, Jalundhwala YJ. The long-term direct and indirect economic burden among Parkinson's disease caregivers in the United States. *Mov Disord*. 2019; 34: 236-245.
9. Martinez-Martin P, Macaulay D, Jalundhwala YJ. The long-term direct and indirect economic burden among Parkinson's disease caregivers in the United States. *Mov Disord*. 2019; 34: 236-245.
10. Classification and Approach to Movement Disorders Chapter: Classification and Approach to Movement Disorders Author(s): Paul E. Youssef Kenneth J. Mack and Kelly D. Flemming.
11. Oxford Textbook of Movement Disorders Edited by David Burn Publisher: Oxford University Press Print Publication Date: Oct 2013 Approach to History Taking and Examination of the Movement Disorder Patient Chapter: Approach to History Taking and Examination of the Movement Disorder Patient Author(s): David J. Burn.
12. Meara J, Bhowmick BK, Hobson P. Accuracy of diagnosis in patients with presumed Parkinson's disease. *Age Ageing*. 1999; 28: 99-102.
13. Katzenschlager R, Cardozo A, Avila Cobo MR, Tolosa E, Lees AJ. Unclassifiable parkinsonism in two European tertiary referral centres for movement disorders. *Mov Disord*. 2003; 18: 1123-1131.
14. Friedman JH, Fernandez HH, Trieschmann MM. Parkinsonism in a nursing home: underrecognition. *J Geriatr Psychiatry Neurol*. 2004; 17: 39-41.
15. Han J, Jain S. Clinical Presentation and Prognosis of Common Movement Disorders. *Prog Neurol Surg*. 2018; 33: 25-40.
16. Munhoz RP, Werneck LC, Teive HA. The differential diagnoses of parkinsonism: findings from a cohort of 1528 patients and a 10 years comparison in tertiary movement disorders clinics. *Clin Neurol Neurosurg*. 2010; 112: 431-435.
17. Elia AE, Lalli S, Albanese A. Differential diagnosis of dystonia. *Eur J Neurol*. 2010; 17: 1-8.
18. Gómez-Río M, Caballero MM, Górriz Sáez JM, Mínguez-Castellanos A. Diagnosis of Neurodegenerative Diseases: The Clinical Approach. *Curr Alzheimer Res*. 2016; 13: 469-474.
19. Santiago JA, Potashkin JA. A network approach to clinical intervention in neurodegenerative diseases. *Trends Mol Med*. 2014; 20: 694-703.

20. Iliffe S, Wilcock J. The UK experience of promoting dementia recognition and management in primary care. *Großbritanniens Erfahrung mit der Förderung der Früherkennung von Demenz und dem Management in der Primärversorgung. Z Gerontol Geriatr.* 2017; 50: 63-67.
21. Akpan A, Tabue-Teguio M, Fougère B. Neurocognitive Disorders: Importance of Early/Timely Detection in Daily Clinical Practice. *J Alzheimers Dis.* 2019; 70: 317-322.
22. Mahlknecht P, Gasperi A, Djamshidian A. Performance of the Movement Disorders Society criteria for prodromal Parkinson's disease: A population-based 10-year study. *Mov Disord.* 2018; 33: 405-413.
23. Strafella C, Caputo V, Galota M. Application of Precision Medicine in Neurodegenerative Diseases. *Front Neurol.* 2018; 9: 701.
24. Tse W, Libow LS, Neufeld R. Prevalence of movement disorders in an elderly nursing home population. *Arch Gerontol Geriatr.* 2008; 46: 359-366.
25. Seraji-Bzorgzad N, Paulson H, Heidebrink J. Neurologic examination in the elderly. *Handb Clin Neurol.* 2019; 167: 73-88.
26. Ringel SP. The practice of neurology: Looking ahead by looking back. *Neurology.* 2015; 84: 2086-2091.
27. Gajos A, Dąbrowski J, Biełkiewicz M, Plachcińska A, Kuśmierk J, Bogucki A. Should non-movement specialists refer patients for SPECT-DaTSCAN?. *Neurol Neurochir Pol.* 2019; 53: 138-143.
28. Wieske L, Richard E, Wijers D, Stam J, Smets EM, Vergouwen MD. Long-term satisfaction after neurological second opinions and tertiary referrals. *Eur J Neurol.* 2011; 18: 1310-1316.
29. Naley M, Elkind MS. Outpatient training in neurology: history and future challenges. *Neurology.* 2006; 66: E1-E6.
30. Zinchuk AV, Flanagan EP, Tubridy NJ, Miller WA, McCullough LD. Attitudes of US medical trainees towards neurology education: "Neurophobia" - a global issue. *BMC Med Educ.* 2010; 10: 49.
31. Burneo JG, Jenkins ME, Bussièrè M. UWO Evidence-Based Neurology Group. Evaluating a formal evidence-based clinical practice curriculum in a neurology residency program. *J Neurol Sci.* 2006; 250: 10-19.
32. Shrubsole K. Implementation of an integrated multidisciplinary Movement Disorders Clinic: applying a knowledge translation framework to improve multidisciplinary care. *Disabil Rehabil.* 2019; 1-13.
33. Qamar MA, Harington G, Trump S, Johnson J, Roberts F, Frost E. Multidisciplinary Care in Parkinson's Disease. *Int Rev Neurobiol.* 2017; 132: 511-523.
34. Dressler D. Nonprimary dystonias. *Handb Clin Neurol.* 2011; 100: 513-538.
35. Schrag A, Anastasiou Z, Ambler G, Noyce A, Walters K. Predicting diagnosis of Parkinson's disease: A risk algorithm based on primary care presentations. *Mov Disord.* 2019; 34: 480-486.
36. Jinnah HA, Albanese A, Bhatia KP. Treatable inherited rare movement disorders. *Mov Disord.* 2018; 33: 21-35.
37. Netravathi M, Pal PK, Indira Devi B. A clinical profile of 103 patients with secondary movement disorders: correlation of etiology with phenomenology. *Eur J Neurol.* 2012; 19: 226-233.
38. Hallett M. Functional (psychogenic) movement disorders - Clinical presentations. *Parkinsonism Relat Disord.* 2016; 22: S149-S152.
39. Thenganatt MA, Jankovic J. Psychogenic (Functional) Movement Disorders. *Continuum (Minneapolis).* 2019; 25: 1121-1140.
40. Höllerhage M. Secondary parkinsonism due to drugs, vascular lesions, tumors, trauma, and other insults. *Int Rev Neurobiol.* 2019; 149: 377-418.
41. Pringsheim T, Barnes TRE. Antipsychotic Drug-Induced Movement Disorders: A Forgotten Problem? *Can J Psychiatry.* 2018; 63: 706743718786702.
42. Zádori D, Veres G, Szalárdy L, Klivényi P, Vécsei L. Drug-induced movement disorders. *Expert Opin Drug Saf.* 2015; 14: 877-890.
43. Caroff SN, Campbell EC. Drug-Induced Extrapyramidal Syndromes: Implications for Contemporary Practice. *Psychiatr Clin North Am.* 2016; 39: 391-411.
44. Savica R, Grossardt BR, Bower JH, Ahlskog JE, Mielke MM, Rocca WA. Incidence and time trends of drug-induced parkinsonism: A 30-year population-based study. *Mov Disord.* 2017; 32: 227-234.
45. Detweiler MB, Kalafat N, Kim KY. Drug-induced movement disorders in older adults: an overview for clinical practitioners. *Consult Pharm.* 2007; 22: 149-165.
46. Mehta SH, Morgan JC, Sethi KD. Drug-induced movement disorders. *Neurol Clin.* 2015; 33: 153-174.
47. Zádori D, Veres G, Szalárdy L, Klivényi P, Vécsei L. Drug-induced movement disorders. *Expert Opin Drug Saf.* 2015; 14: 877-890.
48. Rajan S, Kaas B, Moukheiber E. Movement Disorders Emergencies. *Semin Neurol.* 2019; 39: 125-136.
49. Touse B. Movement disorder emergencies in the elderly: recognizing and treating an often-iatrogenic problem. *Cleve Clin J Med.* 2008; 75: 449-457.
50. Park HY, Park JW, Sohn HS, Kwon JW. Association of Parkinsonism or Parkinson Disease with Polypharmacy in the Year Preceding Diagnosis: A Nested Case-Control Study in South Korea. *Drug Saf.* 2017; 40: 1109-1118.
51. Jiménez-Jiménez FJ, García-Ruiz PJ, Molina JA. Drug-induced movement disorders. *Drug Saf.* 1997; 16: 180-204.
52. Kalisch Ellett LM, Pratt NL, Kerr M, Roughead EE. Antipsychotic polypharmacy in older Australians. *Int Psychogeriatr.* 2018; 30: 539-546.
53. Diederich NJ, Goetz CG. Drug-induced movement disorders. *Neurol Clin.* 1998; 16: 125-139.
54. Martino D, Karnik V, Osland S, Barnes TRE, Pringsheim TM. Movement Disorders Associated With Antipsychotic Medication in People With Schizophrenia: An Overview of Cochrane Reviews and Meta-Analysis. *Can J Psychiatry.* 2018; 63: 706743718777392.
55. Thenganatt MA, Jankovic J. Psychogenic (Functional) Movement Disorders. *Continuum (Minneapolis).* 2019; 25: 1121-1140.
56. Hallett M, Weiner WJ, Kompolti K. Psychogenic movement disorders. *Parkinsonism Relat Disord.* 2012; 18 Suppl 1: S155-S157.
57. Poewe W, Djamshidian-Tehrani A. Movement disorders in systemic diseases. *Neurol Clin.* 2015; 33: 269-297.
58. Isaac ML, Larson EB. Medical conditions with neuropsychiatric manifestations. *Med Clin North Am.* 2014; 98: 1193-1208.
59. de Groot NS, Burgas MT. Is membrane homeostasis the missing link between inflammation and neurodegenerative diseases?. *Cell Mol Life Sci.* 2015; 72: 4795-4805.
60. Espay AJ. Neurologic complications of electrolyte disturbances and acid-base balance. *Handb Clin Neurol.* 2014; 119: 365-382.
61. Etchegoyen M, Nobile MH, Baez F. Metabolic Syndrome and Neuroprotection. *Front Neurosci.* 2018; 12: 196.
62. Ferreira CR, Hoffmann GF, Blau N. Clinical and biochemical footprints of inherited metabolic diseases. I. Movement disorders. *Mol Genet Metab.* 2019; 127: 28-30.
63. Pedrosa JL, Barsottini OG, Espay AJ. Movement Disorders in Metabolic Disorders. *Curr Neurol Neurosci Rep.* 2019; 19: 7.
64. Mulak A, Bonaz B. Brain-gut-microbiota axis in Parkinson's disease. *World J Gastroenterol.* 2015; 21:10609-10620.
65. Hottman DA, Chernick D, Cheng S, Wang Z, Li L. HDL and cognition in neurodegenerative disorders. *Neurobiol Dis.* 2014; 72: 22-36.
66. Kuiper A, Eggink H, Tijssen MA, de Koning TJ. Neurometabolic disorders are treatable causes of dystonia. *Rev Neurol (Paris).* 2016; 172: 455-464.
67. Grabi D, Auré K, Roze E. Mouvements anormaux et maladies neurométaboliques [Movement disorders and neurometabolic diseases]. *Rev Neurol (Paris).* 2011; 167: 123-134.

68. Sureka B, Bansal K, Patidar Y, Rajesh S, Mukund A, Arora A. Neurologic Manifestations of Chronic Liver Disease and Liver Cirrhosis. *Curr Probl Diagn Radiol*. 2015; 44: 449-461.
69. Woimant F, Djebrani-Oussedik N, Collet C, Girardot N, Poujois A. The hidden face of Wilson's disease. *Rev Neurol (Paris)*. 2018; 174: 589-596.
70. McGuire S, Chanchani S, Khurana DS. Paroxysmal Dyskinesias. *Semin Pediatr Neurol*. 2018; 25: 75-81.
71. Aggarwal A, Bhatt M. Advances in Treatment of Wilson Disease. *Tremor Other Hyperkinet Mov (N Y)*. 2018; 8: 525.
72. Chen Y, Haque M, Yoshida EM. Transient improvement of acquired hepatocerebral degeneration with parkinsonian symptoms after failed liver transplant: case report and literature review. *Exp Clin Transplant*. 2011; 9: 363-369.
73. Crichton RR, Dexter DT, Ward RJ. Brain iron metabolism and its perturbation in neurological diseases. *J Neural Transm (Vienna)*. 2011; 118: 301-314.
74. McNeill A, Chinnery PF. Neurodegeneration with brain iron accumulation. *Handb Clin Neurol*. 2011; 100: 161-172.