Identifying and Managing Drug Induced Parkinsonism: The Role of Neuroscience Nurses

Dr. Linda Nichols [1#]
0000-0003-3711-993X

Dr. Jane Alty [2]
0000-0002-5456-8676

1. RN, PhD (Collage of Health and Medicine, University of Tasmania) # Corresponding author
2. FRCP (UK) FRACP MD (A/Professor of Neurology, University of Tasmania. Staff Specialist in Neurology and Stroke, Royal Hobart Hospital Australia

Abstract

Drug induced parkinsonism (DIP) is one of the most frequently occurring side effects of dopamine-receptor blocking agents such as antipsychotic (neuroleptic) and antiemetic drugs. It typically presents with extrapyramidal signs, such as slowed movements, reduced facial expression and muscle stiffness. In contrast to Parkinson's disease, which is caused by a progressive degeneration of pre-synaptic dopaminergic neurons that project from the substantia nigra in the brainstem, DIP is thought to usually occur due to the post-synaptic antagonism of dopamine receptors in the striatum. However, the two conditions can sometimes be clinically indistinguishable, and may even occur together, and thus it can be challenging to make an accurate diagnosis of DIP. It is important to consider DIP in the differential diagnosis of any person with extrapyramidal signs within the context of recent medication changes as the condition is reversible when the offending drug is withdrawn and, without early identification, there is substantial risk of increased morbidity, complications such as falls, and poor quality of life. Recent advancements in cerebral imaging have improved diagnostic accuracy but this technology is costly and not widely available.

There is a dearth of literature pertaining to the role of neuroscience nurses and DIP. This is concerning as the potential for DIP presentations to occur within the neuroscience setting is high. Neuroscience nurses, particularly those working within the movement disorder speciality areas, need the skills to advocate and pursue further investigation for patients who present with extrapyramidal signs, especially if these begin in the context of the prescription of dopamine-blocking drugs. This review is written primarily for neurosciences nurses but will be applicable to a wide range of healthcare workers; it aims to outline potential causative drugs, risk factors and the key clinical characteristics of DIP. It also highlights useful features that help distinguish DIP from Parkinson's disease, summarises investigations and discusses management and care.

KEYWORDS: Parkinson's disease, parkinsonism, drug-induced, neuroleptics, dopamine, nursing, neuroscience nursing.

Acknowledgements: None Funding support: None Conflicts of interest: None

Introduction

Parkinsonism is an umbrella term for a clinical syndrome of bradykinesia (slowed irregular movements) with at least one of the following: muscle rigidity (stiffness), tremor and postural instability (balance problems) (Hughes, Daniel, Kilford, & Lees, 1992; Postuma et al., 2015). There are many different causes of parkinsonism and the most common is Parkinson's disease, which affects about 1-5% of adults over 60; incidence increases with age but about 20% of people diagnosed with Parkinson's are under 50 (Draoui, El Hiba, Aimrane, El Khiat, & Gamrani, 2020; Kowal, Dall, Chakrabarti, Storm, & Jain, 2013; Reeve, Simcox, & Turnbull, 2014).

Questions or comments about this article should be directed to: Linda Nichols

Linda.nichols@utas.edu.au

DOI: 10.21307/ajon-2024-006

It is a degenerative, progressive brain disorder whereby dopaminergic neurons projecting from the substantia nigra in the brainstem gradually die off and this leads to a presynaptic reduction of dopamine release in the striatum. In contrast, drug induced parkinsonism (DIP) occurs when dopamine receptor blocking agents, such as antipsychotic (neuroleptic) and antiemetic drugs, bind to post-synaptic receptors in the striatum and thus stop dopamine having a stimulating effect; see Figure 1. It is generally reversible once the offending drug is withdrawn.

DIP is the second leading cause of parkinsonism (Rissardo & Caprara, 2023), accounting for about 11.9% of all cases with an estimated prevalence of 3.3 per 100,000 person years (Martí□Massó & Poza, 1998; Savica et al., 2017). However, DIP is under-recognised so calculations of prevalence are likely to be an underestimate of the true numbers (Undeberg, McKeirnan, & Easley, 2022). The similarity of its clinical phenotype with Parkinson's disease results in common misdiagnosis with an estimated 6.8% of individuals initially diagnosed with Parkinson's disease later diagnosed as having DIP (Mukilan, Praveen, Chowdary, & Aanandhi, 2018). High rates of misdiagnosis and similar presentations have resulted in a rise in the number of individuals with DIP presenting to movement disorder clinics, neuroscience wards and community-based services (Esper & Factor, 2008; Gershanik, 1994; Shin & Chung, 2012).

Neuroleptic drugs, which are also called antipsychosis drugs, are the most common class of medication associated with DIP (de Germay, Montastruc, Carvajal, Lapeyre-Mestre, & Montastruc, 2020). Once limited to the mental health setting, specifically for schizophrenia and other causes of psychosis, the prescription of neuroleptics are now being increasingly indicated for a much wider range of conditions including depression, anxiety, insomnia, and post-traumatic stress disorder (Gallagher & Bouchard, 2023; Rogers, Hartigan, & Sanders, 2021). Neuroleptic drugs have a multitude of pharmacological actions but generally they all block dopamine receptors. As an estimated 15-60% of individuals on long-term neuroleptics will potentially develop DIP symptoms (Mukilan et al., 2018) this often associated with medication or dosage changes, it is vital that neuroscience nurses remain abreast of current research enabling them to provide appropriate and personalised care for those with parkinsonism. DIP sits in limbo between neurology and psychiatry, and it is this crossover of specialities that makes the diagnosis, management, and personalisation of DIP care particularly challenging. Furthermore, DIP is just one presentation in a range of neuroleptic induced movement disorders that include dystonia, akathisia, catatonia, neuroleptic malignant syndrome and tardive dyskinesia (Caroff et al., 2018); noting that aspects of these movement disorders may also occur in conjunction with DIP. It is imperative that all individuals presenting with new parkinsonism are assessed for DIP, given its high burden related not only to diagnostic workups, potential hospitalisations and healthcare expenditures, but also the personal costs including lost workdays, complications such as falls and poor quality of life (Pitton Rissardo & Caprara, 2023).

Neuroscience nurses play a pivotal role in improving health outcomes for those with parkinsonism. It is important that they know how to provide personalised care for individuals with DIP and lower the risk of complications. The purpose of this article is to provide information to neuroscience nurses about

causative drugs and risk factors for DIP.

It also aims to highlight typical clinical characteristics and useful features that help distinguish DIP from Parkinson's disease. Finally, this review will summarise investigations and discuss care and management.

Causative Medications

The pharmaceutical mechanisms resulting in DIP are varied, but most causative drugs result in blockade of Dopamine D2 receptors in the striatum (Burkhard, 2014; López-Sendón, Mena, & G de Yébenes, 2013; Mukilan et al., 2018). The striatum is a cluster of interconnected nuclei that form a part of the basal ganglia and are critical in the control of motor, reward, and executive function (Bamford & Bamford, 2019). The propensity for a drug to cause DIP is related to its occupancy of D2 receptors (Hirose, 2006). Figure 1 is a schematic diagram of dopaminergic neurons in the striatum. The diagram illustrates the release and binding of dopamine in a healthy state compared to the differing pathophysiology in Parkinson's disease and DIP. In Parkinson's disease there is pre-synaptic degeneration and associated lack of dopamine, this compared to DIP where the post synaptic D2 receptors are blocked by the offending drug.

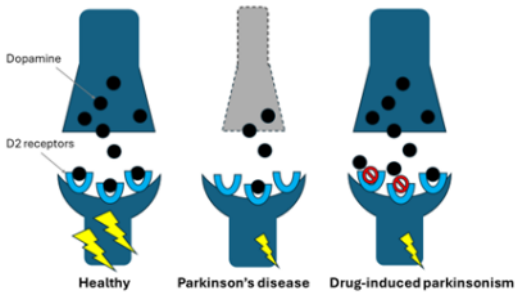

Figure 1: A schematic of dopaminergic neurons in the striatum.

The pre-synaptic neurons project from the substantia nigra to the striatum and release dopamine into the synaptic cleft. In the healthy state, dopamine binds to post-synaptic dopamine (D) receptors and this stimulates the post-synaptic neuron. In Parkinson's disease, there is a lack of dopamine due to pre-synaptic degeneration. In drug-induced parkinsonism, the offending drug typically blocks the post-synaptic D2 receptors, and this blocks the action of dopamine, which leads to less post-synaptic stimulation.

First-generation antipsychotic medications such as Chlorpromazine strongly block the receptors and are frequently associated with DIP (Burkhard, 2014; Pandey et al., 2023) whereas second generation, or so-called 'atypical' antipsychotics including Olanzapine and Risperidone have a lesser risk due to their lower affinity for D2 receptors (Druschky et al., 2020). Nevertheless up to 20% of individuals receiving long term treatment with atypical antipsychotics will develop DIP and, generally the higher the dose of any dopamine-receptor blocking drug, the higher the risk of DIP (Diaz-Martinez et al., 1998; Shin & Chung, 2012).

Not all drugs that cause DIP are directly related to D2 blockade though. For example Lithium Carbonate, which is increasingly common within the neuroscience setting, as it is used for the prevention of cluster headaches and augmentation of antidepressants (López-Sendón, Mena, & G de Yébenes, 2013), is thought to act by decreasing dopamine levels in the striatum or through increased cholinergic activity (Holroyd & Smith, 1995). Although Lithium Carbonate has an indirect dopamine effect, it has a high risk for potentiation and polypharmacy resulting in DIP (Beaulieu & Caron, 2008; Fountoulakis, Tohen, & Zarate Jr, 2022). Other drugs associated with DIP are outlined in Table 1 and include antiemetics, antiepileptic drugs, antiarrhythmics,

Table 1. Drug classes and pharmaceutical agents associated with DIP

Pharmaceutical Agents Frequently Associated with DIP	
Typical Antipsychotics	Chlorpromazine, Prochlorperazine, Promethazine, Fluphenazine, Haloperidol, Primozide, Sulpiride
Atypical Antipsychotics	Olanzapine, Risperidone, Ziprasidone, Aripiparazole, Clozapine, Quetiapine
Anti-emetics	Metoclopramide, Domperidone, Itopride
Dopamine Depleters	Reserpine, Tetrabenazine
Calcium-Channel Blockers	Flunarizine, Cinnarizine
Pharmaceutical Agents Less Frequently Associated with DIP	
Mood Stabilizers	Lithium Carbonate
Antiepileptics	Valproic acid, Phenytoin, Levetiracetam
Anti-hypertensives	Diltiazem
Antidepressants	Paroxetine, Sertraline, Fluoxetine
Antiarrhythmics	Amiodarone, Procaine
Statins	Lovastatin
Immunosuppressants	Ciclosporin, Tacrolimus
Antivirals	Acyclovir, Vidarabine
Antibacterials	Sulfamethoxazole, Trimethoprim
Antifungals	Amphotericin B

Adapted from the following tables: (Adis Editors, 2012; Shin & Chung, 2012; Vasquez Builes, Salazar, Tieck-Fernández, Rojas-Gallego, & Díaz Silva, 2021)

antidepressants, and many other compounds including recreational drugs (Burkhard, 2014; Gallagher & Bouchard, 2023; López-Sendón et al., 2013; Pandey et al., 2023).

Clinical features

The presenting symptoms and signs of DIP are variable, with an extrapyramidal syndrome of slowness and muscle stiffness the key consistent factors. A range of early clinical features include akinesia (freezing), bradykinesia (slowness and irregular rhythm of movements), postural instability, reduced facial expression and blink frequency, tremor, amimia (inability to express ideas by means of gestures or signs) and loss of arm swing when walking (Kumsa, Agenagnew, Alemu, & Girma, 2020; López-Sendón, Mena, & G de Yébenes, 2013). The neurological deficits that individuals experience can be distressing and significant enough to impact activities of daily life (Mukilan, Praveen, Chowdary, & Aanandhi, 2018) such as walking, driving, undertaking usual daily activities and living independently.

Whilst the motor symptoms of DIP and Parkinson's disease may be similar, there are some features that may help differentiate the two.

Table 2: Differentiating features of Parkinson's disease and DIP

Feature	Parkinson's Disease	Drug Induced Parkinsonism (DIP)
Age of Onset	Sixth decade (but 20% are <50 years old)	Variable
Sex	More common in males	Uncertain
Onset	Chronic	Acute or subacute
Symptom Onset	Unilateral or asymmetric	Bilateral and symmetric
Akathisia	Absent	Present
Bradykinesia	Present	Present
Tremor	Rest tremor occurs in 70%	Usually absent or a postural tremor
Rigidity	Progressive and may be marked	Usually mild
Response to Levodopa	Good	Poor
Response to stopping D2 blocking drug	Slight non-sustained improvement then progressive parkinsonism	Good with complete reversal of parkinsonism
DaTscan / VMAT scan	Abnormal: Reduced uptake of presynaptic markers	Normal

DaTscan = dopamine transporter scan (ioflupane), VMAT = vesicular monoamine transporter type 2 (noting that VMAT imaging is currently a research tool).

For example, DIP more frequently presents with a symmetrical motor impairment whereas in Parkinson's disease there is usually one side of the body more affected that the other (see Table 2).

Further, Parkinson's disease is more likely to have a rest tremor in just one hand, whereas DIP often has no tremor or a postural symmetrical tremor (Mena & De Yébenes, 2006). Unlike Parkinson's disease, where the onset of symptoms are typically slow and insidious, developing over months or years, the onset of DIP is fairly rapid and usually within days or weeks of starting a new medication, combining a new medication with an existing one, or following a dose increase (Ali, Sisay, Tariku, Mekuria, & Desalew, 2021; Blanchet & Kivenko, 2016; Kumsa et al., 2020; Undeberg, McKeirnan, & Easley, 2022).

Risk Factors

It is useful for neuroscience nurses to be familiar with the risk factors for DIP so they can be particularly alert to identifying people at higher risk. Established risk factors for developing DIP include dose potency, duration of treatment, polypharmacy and pre-existing extrapyramidal symptoms (López-Sendón, Mena, & de Yébenes, 2012). The roles of demographic risk factors are less certain. For example older age has been identified in the literature as a risk for developing DIP but it is unclear if this may be due to the offending drug 'un-masking' subclinical Parkinson's disease (Moleman et al., 1986). In contrast, other authors argue that younger individuals are at higher risk of DIP (Kasten et al., 2011). For example, Savica et al. (2017) reported that DIP accounted for 73% of parkinsonism presentations in adults aged less than 20 years in their cohort. Other potential risk factors include females which may be due to suppression of dopamine receptors by estrogen (Gordon, Gorski, Borison, & Diamond, 1980) although more recent data suggests males to be a risk (de Germay, Montastruc, Carvajal, Lapeyre-Mestre, & Montastruc, 2020). There may also be a familial and genetic predisposition (Kasten et al., 2011; Rissardo & Caprara, 2023).

Diagnosis

The diagnosis of DIP is based on history, examination and a review of medications (Factor, 2004). Standard imaging and pathology examinations are usually unremarkable. In terms of history, the clinician will specifically ask about typical positive features of DIP such as sudden onset or rapid onset of parkinsonism, symmetry of symptoms/signs and how the symptoms relate to the timing of new medications and dose escalation. They will also seek evidence of historical features that may suggest another cause of parkinsonism such as, for example, REM sleep behaviour disorder and a decreased sense of small (hyposmia), that typically begin years before the motor signs in Parkinson's disease, or visual hallucinations and urinary incontinence that may occur with another parkinsonian conditions such as Dementia with Lewy Bodies (DLB).

The clinician will examine carefully for clinical signs of DIP such as symmetry of extrapyramidal signs; they will look for evidence of bradykinesia, which is often examined through repetitive finger taps, foot taps and gait – and manifests as slow irregular and small movements. Copying of spiral drawings and handwriting provides a useful record of bradykinesia and tremor, that may aid monitoring of improvement over time (Alty, Cosgrove, Thorpe, & Kempster, 2017). The face may have less expression, the voice may be soft and quiet and there may be reduced blink frequency, but these are signs of bradykinesia in general and do not discriminate DIP from PD. They will also examine for muscle rigidity, which is examined by gently moving the limbs, head and trunk whilst assessing tone, again looking to see if this is symmetrical (more common in DIP) or asymmetric (more common in Parkinson's). Tremor is less commonly seen in DIP and when it does occur, tends to be a symmetric 'postural' tremor that is worse when the hands are held outstretched, or when performing an action. The clinician will also perform a careful neurological examination, looking for other rarer causes of parkinsonism such as abnormal eye movements seen in Progressive Supranuclear Palsy (PSP), cerebellar signs seen in Multiple System Atrophy (MSA), and cortical sensory loss and myoclo-

Table 3. Guide to the Diagnostic Approach to Suspected DIP

• No previous history of parkinsonism before the prescription of the offending drug.
• Review medical history including past and present medications, assessing for potentiation, polypharmacy and potential drug interactions.
• Consider possible exposure to toxins or recreational drugs.
• Individuals with AIDS have an increased risk of DIP due to loss of neuronal cell bodies.
• Consider the individual's age as Parkinson's disease is less likely in individuals younger than 50 years.
• Review falls in combination with psychotropic administration as medications can lower blood pressure and increase the risk of falls in confused or at-risk patients.
• Review the timeframes associated with the onset of symptoms (usually acute or subacute with DIP). DIP has a temporal relationship with new medications and can occur within days of commencing a new drug, although in some cases it may be months prior to the onset of symptoms.
• Assess for signs and symptoms that are inconsistent with DIP including unilateral symptoms, significant axial impairment, freezing gait, hyposmia, or tremor.
• DIP is generally characterised as bilateral and symmetric parkinsonism.
• Response to levodopa is limited in DIP, yet diagnostically useful in Parkinson's disease.
• Consider DaT scan, single proton emission computerized tomography (SPECT) particularly in cases where symptoms have not resolved within six months of ceasing offending drugs.
• Consider a comorbid or alternative diagnosis.

nus seen in corticobasal syndrome (CBS). Any 'red flags' such as an abnormal sensory exam, abnormal eye movements or autonomic dysfunction would alert the clinician to look harder for a secondary diagnosis as DIP would not entirely explain these findings (recognising that it is possible to have DIP and a second neurological diagnosis); see Table 3.

Vascular parkinsonism deserves a special mention as this condition can present almost identically to DIP and may occur concurrently. It is caused by a combination of small vessel disease and small strokes that disrupt the fronto-striatal pathways. It typically presents with a symmetrical parkinsonism, that may be of sudden/rapid onset, but may be differentiated from DIP in that it tends to cause "lower half parkinsonism"; this manifest as gait being disproportionately impaired with small, slowed steps which have been termed

"magnetic gait" or "walk of the little steps" ('marche a petit pas') whereas the upper limbs and face may appear relatively unaffected (Korczyn, 2015). Individuals with vascular parkinsonism may also have other frontal lobe motor and cognitive features such as impaired executive cognitive function and primitive reflexes such as a palmar-mental reflex or grasp reflex (Benítez-Rivero et al., 2014).

A prompt diagnosis is imperative as a delayed diagnosis is associated with ineffective treatment and reduced quality of life (Pitton Rissardo & Caprara, 2023). The gold standard for diagnosing DIP is to cease the offending agent and to monitor the individual for improvements and a reversal of symptoms (Lim et al., 2013). However, there is a lack of consensus regarding the duration of recovery post the cessation of a potentially causative drug. The remittance period, to allow motor symptoms to recover, is estimated to be within days to weeks. However an estimated 30% of individuals may continue to show persisting symptoms beyond this time (Blanchet & Kivenko, 2016; López-Sendón, Mena, & de Yébenes, 2012) ; see Case Study box . The reversal of symptoms may be further complicated by an individual's clinical dependence on a medication, and it is often a balancing act between alleviating symptoms of DIP and managing the underlying condition, particularly in the setting of chronic severe mental health diagnoses where the interruption of treatment is not generally advisable unless under direct medical supervision in an inpatient setting (Galoppin et al., 2020).

CASE STUDY

A 45-year-old female was admitted to the ward for management of migraine. She also had a diagnosis of severe depression, and this was managed with a combination of Lithium Carbonate, Olanzapine and Chlorpromazine. She had been taking these prescribed medications for 3 years and the dose of chlorpromazine had been recently increased. Within a period of one to two weeks of the dose increase, there was a marked loss of walking speed including a loss of arm swing, with akathisia, bradykinesia, and mild rigidity. Notably the clinical signs were asymmetric and not typical of DIP. Given the sudden onset of signs and symptoms, she had an MRI brain scan, and this was normal. Concerns were raised about possible DIP and so the dose of chlorpromazine was reduced. The anticholinergic drug Benztropine was prescribed for presumed DIP, but there was little improvement over the first four weeks. A brain Vesicular monoamine transporter (VMAT), positron emission tomography (PET)/ computerized tomography (CT) study was undertaken to make sure there was no underlying neurodegenerative cause for the parkinsonism; this demonstrated a normal and symmetrical elevated uptake of tracer, with no evidence of loss of the nigrostriatal dopaminergic pathway. Recovery was aided by allied health input including physiotherapy and occupational therapy and she completely recovered over the next 2 months.

Misdiagnosis rates of DIP

It is important to accurately diagnose DIP as it is usually completely reversible once the causative medication is removed. It is clinically recommended that any new parkinsonism presentation be assessed for potential pharmaceutical causes, this necessitating a complete medication evaluation of all individuals presenting with suspected parkinsonism symptoms. (DeMaagd & Philip, 2015). It is estimated that DIP represents 3-12% of all parkinsonism presentations within the neuroscience setting (Alves et al., 2009; Martí□ Massó & Poza, 1998; Meara, Bhowmick, & Hobson, 1999; Savica et al., 2017). Of these presentations, the rates of initial misdiagnosis for DIP are estimated to be as high as 40-75%, with the time to diagnosis averaging 1.8 years (Esper & Factor, 2008a; Friedman, Fernandez, & Trieschmann, 2004; Hansen, Brown, Weigel, & Casey, 1992; Stephen & Williamson, 1984). Contributing to these high rates of misdiagnosis is a wide variation in individual susceptibility and initial presentation. When the diagnosis is uncertain, and the symptoms could be indicative of Parkinson's disease, (Kaegi, Bhatia, & Tolosa, 2010) the use of dopamine transporter imaging such as DaT Scans (see Figure 2 example) may aid differentiation of DIP from degenerative causes of parkinsonism (Rissardo & Caprara, 2023). In degenerative parkinsonism, these scans show a reduction in the presynaptic striatal terminals but in DIP these scans are normal. However, it is important to note that these imaging modalities are not specific for PD and will also be abnormal in other neurodegenerative disorders such as PSP, MSA, CBS and DLB. This imaging technology is an effective means to support an accurate diagnosis. However, it remains unattainable for most due to high costs, lack of availability (with most imaging technology located in larger cities) and it is also invasive, requiring the injection of a radionuclide.

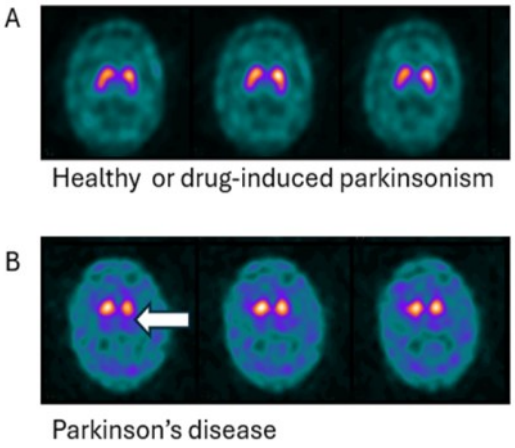

Figure 2. DaTscan (FP-CIT SPECT): the images demonstrate the density of pre-synaptic dopaminergic neurons in the striatum. In the healthy state and in drug-induced parkinsonism, there is no loss of pre-synaptic dopaminergic neurons, and the striatum is a normal 'comma' shape. In Parkinson's disease (and some other degenerative disorders), there is a loss of pre-synaptic dopaminergic neurons in the putamen (white arrow) and the striatum looks like a "full stop" shape. Later in the disease, with further progressive degeneration, the 'full stop' shape also disappears.

Table 4. Differential diagnoses of DIP

Neurodegenerative disorders	**Other conditions**
Parkinson's disease	Vascular parkinsonism
Progressive Supranuclear Palsy	Functional neurological disorder
Multisystem Atrophy	Hyperthyroidism
Corticobasal Syndrome	Benzodiazepine withdrawal
Dementia with Lewy bodies	Infective and autoimmune encephalitis

Adapted from the following tables: (Alves, Forsaa, Pedersen, Gjerstad, & Larsen, 2008; Dallapiazza et al., 2018; Sethi, 2003)

In all presentations that do not resolve, a differential diagnosis needs to be considered. It is possible that DIP may occur together with a second diagnosis, especially vascular parkinsonism, and Parkinson's disease, and that withdrawing the offending drug will thus only relieve part of the clinical features. Table. 4 outlines the potential differential diagnoses for DIP.

Treatment and Care

Treatment of DIP should be individualised and consider varied vulnerabilities and medication priorities as well as the impact on activities of daily living and quality of life. The primary treatment of DIP specifically focuses on prevention, avoidance and the cessation of the offending drugs (Powell, Gallur, Koopowitz, & Hayes, 2020). Neuroscience nurses are critical and play a key role in promoting health, managing complications, and assisting individuals to adapt to the limitations of their disease (Chen, Lu, Jiang, & Huang, 2021).

The avoidance of causative drugs, or substitution with drugs that have a safer profile, is not always tenable as individuals may be clinically dependent on medications, and there is often a delicate balance between ameliorating parkinsonism symptoms and avoiding relapse of the underlying conditions such as depression or schizophrenia. Ultimately an individual may advocate for the continued prescription of the potential causative agent due to the underlying severity and refractory nature of their illness. In this case individual wishes need to be respected, however ongoing monitoring and counselling should occur (Undeberg, McKeirnan, & Easley, 2022), noting that some individuals may not be forthcoming with details related to their symptoms in fear of their medication regime changing.

It is imperative that potentially causative medications are reviewed and discontinued where possible, as outcome is dependent on drug exposure and early discontinuation is associated with more positive outcomes (Anand et al., 2023) than a delayed reduction or cessation of the drug (Rissardo & Caprara, 2023). Regular reviews of medication profiles should also occur with potentially causative agents flagged for potential discontinuation or change to an alternative agent as new therapies become available (Undeberg et al., 2022). Once a causative agent is discontin-

ued, parkinsonism symptoms usually resolve within six months (Brigo, Erro, Marangi, Bhatia, & Tinazzi, 2014; Tachibana et al., 2020).

Pharmacological approaches to DIP commonly involve the use of centrally acting anticholinergic agents such as Benztropine or Amantadine that are used to improve rigidity (Friedman, 2014). Despite the longstanding history of anticholinergic use in the treatment of DIP, there is a lack of data to support their effectiveness and treatment decisions needs to be on an individual basis (Ahlenius & Ericson, 2001). In the setting of refractory DIP there is anecdotal evidence that electroconvulsive therapy can temporarily ameliorate parkinsonism and may also aid in the treatment of psychosis and depression (Baez & Avery, 2011; Faber & Trimble, 1991). The use of Levodopa generally produces a limited response in DIP due to striatal D2 receptor blockage (Burkhard, 2014; López-Sendón, Mena, & de Yébenes, 2012).

Psychological support is imperative as individuals are often vulnerable due to pre-existing mental illness and traumatised by the rapid onset of motor symptoms. A multidisciplinary team approach is intuitive for personalised care and neuroscience nurses fulfill several vital roles including the enabling of an integrated flow of care (Prell et al., 2020; Radder et al., 2019). The key components of any care model is that it is holistic, interdisciplinary, integrated, patient centred and personalised (van Munster et al., 2022).

Conclusion

This paper addresses knowledge gaps and aids neuroscience nurses in the timely identification of DIP, its treatment and care. This requires knowledge of possible offending drugs and the signs and symptoms of both DIP and Parkinson's disease. Neuroscience nurses have a duty to remain vigilant to the possibility of DIP and to have the skills to manage it appropriately when present. Nurses can work with individuals throughout the course of their illness. The prevalence of DIP is increasing and despite this it is a frequently overlooked and a neglected topic.

References

Adis Editors. (2012). Manage drug-induced parkinsonism through early recognition of the condition and discontinuation of the causative agent. *Drugs & Therapy Perspectives, 28*(12), 20-23. doi:10.1007/BF03262145

Ahlenius, S., & Ericson, E. (2001). Scopolamine does not restore normal conditioned avoidance performance in raclopride-treated rats. *Journal of Neural Transmission, 108*, 415-430.

Ali, T., Sisay, M., Tariku, M., Mekuria, A. N., & Desalew, A. (2021). Antipsychotic-induced extrapyramidal side effects: A systematic review and meta-analysis of observational studies. *Plos one, 16*(9), e0257129.

Alty, J., Cosgrove, J., Thorpe, D., & Kempster, P. (2017). How to use pen and paper tasks to aid tremor diagnosis in the clinic. *Pract Neurol, 17*(6), 456-463. doi:10.1136/practneurol-2017-001719

Alves, G., Forsaa, E., Pedersen, K. F., Gjerstad, M., & Larsen, J. (2008). Epidemiology of Parkinson's disease. *Journal of neurology, 255*, 18-32. doi:10.1007/s00415-008-5004-3

Anand, R., Pandey, S., Garg, R. K., Singh Malhotra, H., Shrivastava, S., Kar, S. K., . . . Rizvi, I. (2023). Phenomenology, quality of life, and predictors of reversibility in patients with drug-induced movement disorders: a prospective study. *CNS Spectr, 28*(5), 534-536. doi:10.1017/s1092852922001201

Baez, M. A., & Avery, J. (2011). Improvement in drug-induced parkinsonism with electroconvulsive therapy. *The American Journal of Geriatric Pharmacotherapy, 9*(3), 190-193.

Bamford, I. J., & Bamford, N. S. (2019). The Striatum's Role in Executing Rational and Irrational Economic Behaviors. Neuroscientist, 25(5), 475-490. doi:10.1177/1073858418824256

Beaulieu, J.-M., & Caron, M. G. (2008). Looking at lithium: molecular moods and complex behaviour. *Molecular interventions, 8* (5), 230.

Benítez-Rivero, S., Lama, M. J., Huertas-Fernández, I., de Toledo, P. Á., Cáceres-Redondo, M. T., Martín-Rodríguez, J. F., . . . Mir, P. (2014). Clinical features and neuropsychological profile in vascular parkinsonism. *Journal of the neurological sciences, 345*(1-2), 193-197.

Blanchet, P. J., & Kivenko, V. (2016). Drug-induced parkinsonism: diagnosis and management. *Journal of parkinsonism and restless legs syndrome*, 83-91.

Bohlega, S., & Al-Foghom, N. B. (2013). Drug-induced Parkinson`s disease. A clinical review. *Neurosciences, 18 3*, 215-221.

Brigo, F., Erro, R., Marangi, A., Bhatia, K., & Tinazzi, M. (2014). Differentiating drug-induced parkinsonism from Parkinson's disease: an update on non-motor symptoms and investigations. *Parkinsonism & related disorders, 20*(8), 808-814.

Burkhard, P. R. (2014). Acute and subacute drug-induced movement disorders. *Parkinsonism & related disorders, 20*, S108-S112.

Caroff, S. N., Mu, F., Ayyagari, R., Schilling, T., Abler, V., & Carroll, B. (2018). Hospital utilization rates following antipsychotic dose reductions: implications for tardive dyskinesia. *BMC psychiatry, 18*, 1-13.

Chen, Y., Lu, T., Jiang, X., & Huang, X. (2021). The effectiveness of specialized nursing interventions for patients with Parkinson disease: A randomized controlled study protocol. *Medicine, 100*(2), e23972.

Cunningham Owens, D. G. (2014). Parkinsonism. In D. G. Cunningham Owens (Ed.), *A Guide to the Extrapyramidal Side-Effects of Antipsychotic Drugs* (2 ed., pp. 68-133). Cambridge: Cambridge University Press.

Dallapiazza, R., Vloo, P., Fomenko, A., Lee, D., Hamani, C., Munhoz, R., . . . Kalia, S. (2018). Considerations for Patient and Target Selection in Deep Brain Stimulation Surgery for Parkinson's Disease. In.

de Germay, S., Montastruc, F., Carvajal, A., Lapeyre-Mestre, M., & Montastruc, J.-L. (2020). Drug-induced parkinsonism: Revisiting the epidemiology using the WHO pharmacovigilance database. *Parkinsonism & related disorders, 70*, 55-59.

Diaz-Martinez, A., Benassinni, O., Ontiveros, A., Gonzalez, S., Salin, R., Basquedano, G., & Martinez, R. A. (1998). A randomized, open-label comparison of venlafaxine and fluoxetine in depressed outpatients. *Clinical therapeutics, 20*(3), 467-476.

Draoui, A., El Hiba, O., Aimrane, A., El Khiat, A., & Gamrani, H. (2020). Parkinson's disease: from bench to bedside. *Revue Neurologique, 176*(7-8), 543-559.

Druschky, K., Bleich, S., Grohmann, R., Engel, R. R., Toto, S., Neyazi, A., . . . Stübner, S. (2020). Severe parkinsonism under treatment with antipsychotic drugs. *European Archives of Psychiatry and Clinical Neuroscience, 270*, 35-47.

Esper, C. D., & Factor, S. A. (2008). Failure of recognition of drug-induced parkinsonism in the elderly. *Movement disorders: official journal of the Movement Disorder Society, 23*(3), 401-404.

Faber, R., & Trimble, M. R. (1991). Electroconvulsive therapy in Parkinson's disease and other movement disorders. *Movement disorders: official journal of the Movement Disorder Society, 6*(4), 293-303.

Factor, S. A. (2004). Lithium-induced movement disorders. *NEUROLOGICAL DISEASE AND THERAPY, 62*, 209-232.

Fountoulakis, K. N., Tohen, M., & Zarate Jr, C. A. (2022). Lithium treatment of Bipolar disorder in adults: A systematic review of randomized trials and meta-analyses. *European Neuropsychopharmacology, 54*, 100-115.

Friedman, J. H. (2014). Challenges in our understanding of neuroleptic induced parkinsonism. *Parkinsonism & related disorders, 20*(12), 1325-1328.

Gallagher, S., & Bouchard, L. (2023). Nurse practitioner educational preparation and confidence related to managing antipsychotic medications and associated drug-induced movement disorders. *Journal of the American Association of Nurse Practitioners*, 10.1097.

Galoppin, M., Berroir, P., Soucy, J. P., Suzuki, Y., Lavigne, G. J., Gagnon, J. F., . . . Blanchet, P. J. (2020). Chronic neuroleptic-induced parkinsonism examined with positron emission tomography. *Movement Disorders, 35* (7), 1189-1198.

Gershanik, O. S. (1994). Drug-induced parkinsonism in the aged: recognition and prevention. *Drugs & aging, 5*, 127-132.

Gordon, J. H., Gorski, R. A., Borison, R. L., & Diamond, B. I. (1980). Postsynaptic efficacy of dopamine: possible suppression by estrogen. *Pharmacology Biochemistry and Behavior, 12*(4), 515-518.

Hirose, G. (2006). Drug induced parkinsonism: a review. *Journal of neurology, 253*, iii22-iii24.

Holroyd, S., & Smith, D. (1995). Disabling parkinsonism due to lithium: a case report. *Journal of Geriatric Psychiatry and Neurology, 8*(2), 118-119.

Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry, 55*(3), 181-184. doi:10.1136/jnnp.55.3.181

Kasten, M., Brüggemann, N., König, I. R., Doerry, K., Steinlechner, S., Wenzel, L., . . . Lencer, R. (2011). Risk for antipsychotic-induced extrapyramidal symptoms: influence of family history and genetic susceptibility. *Psychopharmacology, 214*, 729-736.

Korczyn, A. D. (2015). Vascular parkinsonism—characteristics, pathogenesis and treatment. *Nature Reviews Neurology, 11* (6), 319-326.

Kowal, S. L., Dall, T. M., Chakrabarti, R., Storm, M. V., & Jain, A. (2013). The current and projected economic burden of Parkinson's disease in the United States. *Movement Disorders, 28*(3), 311-318.

Kumsa, A., Agenagnew, L., Alemu, B., & Girma, S. (2020). Psychotropic medications induced parkinsonism and akathisia in people attending follow-up treatment at Jimma Medical Center, Psychiatry Clinic. *Plos one, 15*(7), e0235365.

Lim, T., Ahmed, A., Itin, I., Gostkowski, M., Rudolph, J., Cooper, S., & Fernandez, H. (2013). Is 6 months of neuroleptic withdrawal sufficient to distinguish drug-induced parkinsonism from Parkinson's disease? *Inter-*

national Journal of Neuroscience, 123(3), 170-174.

López-Sendón, J., Mena, M. A., & G de Yébenes, J. (2013). Drug-induced parkinsonism. *Expert opinion on drug safety, 12*(4), 487-496.

López-Sendón, J. L., Mena, M. A., & de Yébenes, J. G. (2012). Drug-induced parkinsonism in the elderly: incidence, management and prevention. *Drugs & aging, 29*, 105-118.

Martí-Massó, J. F., & Poza, J. J. (1998). Cinnarizine-induced parkinsonism: ten years later. *Movement Disorders, 13*(3), 453-456.

Mena, M. A., & De Yébenes, J. G. (2006). Drug-induced parkinsonism. *Expert opinion on drug safety, 5*(6), 759-771. Retrieved from https://www.tandfonline.com/doi/pdf/10.1517/14740338.5.6.759

Moleman, P., Janzen, G., Von Bargen, B. A., Kappers, E. J., Pepplinkhuizen, L., & Schmitz, P. (1986). Relationship between age and incidence of parkinsonism in psychiatric patients treated with haloperidol. *The American journal of psychiatry, 143*(2), 232-234.

Mukilan, D., Praveen, D., Chowdary, P. R., & Aanandhi, M. V. (2018). Drug-induced parkinsonism: a review. *Drug Invent Today, 10* (2), 212-215.

Pandey, S., Pitakpatapee, Y., Saengphatrachai, W., Chouksey, A., Tripathi, M., & Srivanitchapoom, P. (2023). *Drug-Induced Movement Disorders.* Paper presented at the Seminars in Neurology.

Pitton Rissardo, J., & Caprara, A. L. F. (2023). Neuroimaging Techniques in Differentiating Parkinson's Disease from Drug-Induced Parkinsonism: A Comprehensive Review. *Clinics and Practice, 13*(6), 1427-1448.

Pitton Rissardo, J., Vora, N., Mathew, B., Kashyap, V., Muhammad, S., & Fornari Caprara, A. (2023). Overview of Movement Disorders Secondary to Drugs. *Clinics and Practice, 13*, 959-976. doi:10.3390/clinpract13040087

Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., . . . Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders, 30*(12), 1591-1601. doi:https://doi.org/10.1002/mds.26424

Powell, A., Gallur, L., Koopowitz, L., & Hayes, M. W. (2020). Parkinsonism in the psychiatric setting: An update on clinical differentiation and management. *BMJ Neurology Open, 2*(1).

Prell, T., Siebecker, F., Lorrain, M., Tönges, L., Warnecke, T., Klucken, J., . . . Lorenzl, S. (2020). Specialized staff for the care of people with Parkinson's disease in Germany: an overview. *Journal of Clinical Medicine, 9*(8), 2581.

Radder, D. L., de Vries, N. M., Riksen, N. P., Diamond, S. J., Gross, D., Gold, D. R., . . . Lennaerts, H. H. (2019). Multidisciplinary care for people with Parkinson's disease: the new kids on the block! *Expert review of neurotherapeutics, 19*(2), 145-157.

Reeve, A., Simcox, E., & Turnbull, D. (2014). Ageing and Parkinson's disease: why is advancing age the biggest risk factor? *Ageing research reviews, 14*, 19-30.

Rissardo, J. P., & Caprara, A. L. F. (2023). Predictors of Drug-Induced Parkinsonism. *APIK Journal of Internal Medicine*.

Rogers, R., Hartigan, S. E., & Sanders, C. E. (2021). Identifying mental disorders in primary care: diagnostic accuracy of the connected mind fast check (CMFC) electronic screen. *Journal of clinical psychology in medical settings, 28*(4), 882-896.

Savica, R., Grossardt, B. R., Bower, J. H., Ahlskog, J. E., Mielke, M. M., & Rocca, W. A.

(2017). Incidence and time trends of drug-induced parkinsonism: A 30-year population -based study. *Movement Disorders, 32*(2), 227-234.

Sethi, K. D. (2003). *Differential Diagnosis of Parkinsonism*.

Shin, H. W., & Chung, S. J. (2012). Drug-induced parkinsonism. *J Clin Neurol, 8*(1), 15 -21. doi:10.3988/jcn.2012.8.1.15

Tachibana, K., Matsuura, K., Shindo, A., Matsuyama, H., Ii, Y., Taniguchi, A., & Tomimoto, H. (2020). Symptomatic characteristics of parkinson's disease induced by neuroleptic drugs, based on a functional neuroimaging diagnosis. *Internal Medicine, 59*(4), 485-490.

Undeberg, M. R., McKeirnan, K. C., & Easley, D. (2022). Respecting the patient's choice: a case of possible drug-induced parkinsonism. *Pharmacy, 10*(1), 10.

van Munster, M., Stümpel, J., Thieken, F., Ratajczak, F., Rascol, O., Fabbri, M., . . . Pedrosa, D. J. (2022). The role of Parkinson nurses for personalizing Care in Parkinson's disease: a systematic review and Meta-analysis. *Journal of Parkinson's Disease, 12* (6), 1807-1831.

Vasquez Builes, S., Salazar, C., Tieck-Fernández, M., Rojas-Gallego, I., & Díaz Silva, G. (2021). Drug-induced parkinsonism: what should a psychiatrist know? *Revista Mexicana de Neurociencia, 22*. doi:10.24875/RMN.20000010